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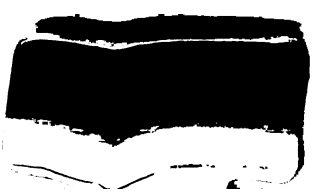

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TRANSACTIONS OF THE

Chicago Pathological Society

From October, 1899, to June, 1901

VOLUME IV

AMERICAN MEDICAL ASSOCIATION PRESS
CHICAGO: NINETEEN HUNDRED AND TWO

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PREFACE

It is probably needless to say that the Publication Committee does not assume responsibility for the different views and statements advanced by the authors of the various articles and reports in this volume.

The Committee desires to express its thanks to the publishers of the following journals for the free use of sundry cuts and plates for illustrations of articles already published by them, and reprinted here: *The New York Medical Journal, The Journal of the Boston Society of Medical Sciences,* and *Medicine.*

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NECROLOGICAL LIST

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Mergler, Marie J. ..... May 8, 1901

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THE CENTRAL NERVOUS SYSTEM.

A PERIENDOTHELIOMA OF THE DURA MATER INVOLVING THE CRANIAL NERVES.

D. R. BROWER AND H. G. WELLS.

Report of Dr. Brower.

Mrs. W., aged forty-seven years, was brought to my clinic, October, 1890, by Dr. Annetta S. Dobbins, with the following history: She was admitted to the Woman's and Children's Hospital, May 28, 1882, complaining of a sense of weariness on the slightest exertion, of an intense earache in the left ear, a severe headache, and pain and swelling of the left side of the face. There was a slight trace of albumin in the urine, and a slight aortic regurgitant murmur. She had had three living children and six miscarriages. Under treatment she improved, and was discharged, June 29, 1882. On January 6, 1883, she returned to the dispensary of the hospital, on account of a distressing and peculiar cough. The following June she again returned to the hospital with a transitory attack of left hemiparesis, the sensory impairment being more marked than the motor, and the cough of the preceding winter more harassing. A month later she had another miscarriage, in which there was an unusual loss of blood. She was again taken to the hospital, and there the facial paralysis was detected, and on examination all the cranial nerves below the fourth except the abducens were found to be involved. On my examination I found paralysis of the motor and sensory branches of the trigeminus on the left side; of the abducens manifested by strabismus, diplopia,

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and dizziness; of the facial, a complete facial paralysis, the muscles showing the reaction of degeneration; the auditory, with a complete loss of hearing; of the glossopharyngeal, shown by a posterior ageusia; of the pneumogastric and spinal accessory, shown by the cough, disturbed respiration and heart's action, alterations in the voice, gastralgia, and difficulty in swallowing; of the hypoglossal, by hemiparalysis and atrophy of the tongue. The only symptom that showed progression of the path-

Fig. 1.—The patient as she appeared at my clinic, December, 1897.

ological condition was the involvement of the abducens, as compared with the record made in 1883. The lesion began in May, 1882, probably slowly progressed, and just when its maximum was attained, after July, 1883, the record does not show. There was at the time of my examination also atrophy of the left sternocleidomastoideus and of the upper part of the trapezius muscles. Albumin was still present in the urine, and a slight aortic regurgitant murmur, and the arteries

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showed marked sclerosis. She had had at this time in all twelve miscarriages. The family history was negative; the mother was still living, and the father had died a few months before of cardiac disease.

We made the diagnosis of meningeal tumor, because the symptoms continued to be unilateral until the end. Nuclear lesions are almost invariably bilateral, or soon become so, and, moreover, there was no progression

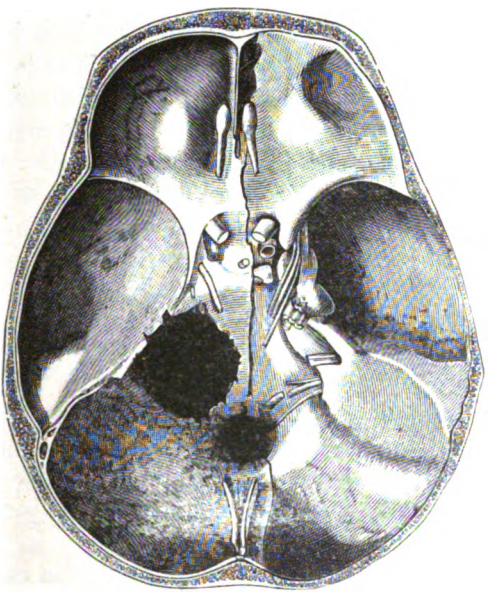

Fig. 2.—The lesion diagrammatically as located at this clinic.

upward or downward. I excluded an amyotrophic lateral sclerosis and progressive bulbar paralysis.

There were at no time in the case any pressure symptoms manifest. Repeated examinations were made of the optic fundus, and nothing abnormal found. Interesting features of the case are, first, its long period of quiescence; beginning with 1890 till the time of her death the case was shown every year at my clinic, and

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the symptoms showed no progression. The growth of the tumor, also, must have been slow. The next interesting fact is the absence of pressure symptoms, and the third interesting one, and the very important one, is the fact that the pathological study of the tumor excludes syphilis in its pathogenesis, and makes it a benign tumor of the perithelial variety. We supposed it was syphilitic, because of her numerous miscarriages, none of which were the product of violence, and because of the marked arterial degeneration which she had, and because of glandular enlargements, and because of the benefit derived from the use of antisyphilitic remedies. She was probably a syphilitic patient with a non-syphilitic brain tumor, and this fact should make us more cautious in referring the genesis of nervous symptoms to syphilis in syphilitic patients.

The patient died of angina pectoris.

Pathological Report by Dr. Wells.

Autopsy was performed twenty-six hours after death by Dr. S. M. White and myself. The body was that of a slenderly-built, poorly-nourished woman. It was noticeable that the mouth was drawn to the right and that the left cheek was thinner through its substance than the right. The chief findings in the body were the following:

1. A marked general arterio-sclerosis, seen especially in the larger branches, such as the splenic and coronaries, which were calcified into unyielding, tortuous tubes.

2. Calcification of the aortic valves, without incompetence to the water test or stenosis.

3. Hypertrophy of the left ventricle.

4. Advanced chronic interstitial nephritis.

5. A neoplasm of the dura, extending into the petrous portion of the left temporal bone.

6. Left hemiatrophy of the facial muscles and of the tongue.

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Nowhere in the body could lesions characteristic of syphilis be found, although on account of the history of the case and the provisional diagnosis they were looked for most carefully. The extensive arterio-sclerosis and the calcification of the aortic valves could have been syphilitic, but were not necessarily so.

On opening the cranial cavity nothing abnormal was found over the surface covered by the calvarium. The left inferior posterior fossa, however, was found to be occupied by a mass binding the dura firmly to the skull, less so to the brain. The dura, brain, and tumor mass were removed *in toto* by cutting the growth out of the petrous bone. It was found that this bone had been invaded anteriorily as far as the foramen lacerum medium and along the superior border of the petrous portion of the temporal, and posteriorly to the margin of the foramen magnum, although not into it. The mastoid process had disappeared. This location and extent, it will be noticed, exactly agrees with the provisional location determined from the clinical findings as shown in Fig. 2.

On complete removal the tumor was found to consist of a dense tissue, resembling fibrous tissue in most places. although toward the median line were several softer, reddish, nodular masses. The greatest length of the tumor is antero-posteriorly, this diameter measuring 6.5 cm.; transversely it measures 4 cm., and the same in thickness. More of the growth is external than internal to the dura mater, which seems to bisect it. Its superior surface is in contact with the inferior surface of the left cerebellar hemisphere and the posterior portion of the tempero-sphenoidal lobe, but it is not adherent to the brain nor to the pia mater. It is held attached to the brain by the vessels and nerves entering its substance. On the internal surface it is in contact with the pons and the anterior half of the medulla. It is quite plain why the paralysis involved just the nerves it

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did—the fifth to the twelfth inclusive. The fourth, rising from its deep nucleus in the floor of the aqueduct of Sylvius, and emerging in front of the pons from the outer side of the crus, would escape any direct pressure from the growth. On the other hand, the fifth, emerging from the lateral aspect of the pons, would be pressed upon at this point, and also as far forward as the Gasserian ganglion. Similarly all the other nerves behind the fifth would be destroyed. Unfortunately, during the removal of the brain the nerves behind the third were torn from the brain at their roots, so that the changes in them can not be studied.

Connecting the growth to the brain are the anterior and inferior cerebellar arteries and small branches from the left vertebral. Anteriorly the internal carotid enters and courses backward and internally in its substance to emerge near the inner anterior angle. Its walls are much thickened (sclerotic), but not invaded by the tumor tissue, in which it lies in a distinct sheath, nor does the lumen seem lessened by pressure.

The left lobe of the cerebellum is atrophied so that only the posterior half remains, and this remnant is pushed to the right so that its middle line corresponds to the right edge of the medulla, the left tonsillar lobe lying over the lower end of the fourth ventricle. The left temporo-sphenoidal lobe is flattened so that it is about two-thirds the size of the right; this is the result of the lessening in size of the convolutions rather than to a disappearance of them. The medulla is pushed slightly to the right, and the left olive seems smaller than its fellow. The left half of the pons is greatly atrophied, being but 7 to 10 mm. in thickness, while the right is 12 to 18 mm. thick. This atrophy involves the entire left side of the pons. A special study of the changes in the central nervous system will be reported subsequently.

On cross-section the tumor is found to be exceedingly

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vascular, in some portions almost spongy with blood vessels. The peripheral portions are less vascular than the central and more fleshy, the center being rather fibrous. In consistency it is firm, but quite elastic. Many minute granules of calcified material are present near the center, but absent in the periphery, barely visible to the naked eye as clear, sand-like particles. Except where torn in removal from the bone the growth is distinctly surrounded by a thin, fibrous capsule. The dura loses its identity in the tumor, no traces of it being visible on the cut surface.

Microscopically the different portions of the tumor vary slightly in structure, but are made up in varying portions of blood vessels, which are always numerous, stroma, and tumor cells. For the most part the vessels are the prominent feature, for in some sections they are so numerous as to resemble an angioma. This is especially true of the peripheral portions of the growth. In the center the vessels are larger, generally surrounded by considerable connective tissue, and but few of the small vessels are to be seen.

The larger vessels have walls consisting of an internal layer of endothelium and a series of laminæ of connective tissue surrounding it, with apparently no muscular tissue. They differ from the smaller vessels solely in size and in the amount of connective tissue in their walls. The very smallest capillaries always possess these two layers, an internal lining of endothelium and a layer of connective tissue, which may, however, consist of but little more than a basement membrane supporting the endothelium. No changes were seen in the endothelium, which is identical with that of adult vessels; nowhere is it found proliferating. In proportion to the thickness of their walls the lumen of the smaller vessels is large, so that they resemble the vessels of granulation tissue (Fig. 3).

In the peripheral and most vascular portions the

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numerous vessels are entirely surrounded by the tumor cells, which fill all the space between them in such a way that it might be said either that the tumor cells form the stroma for the vessels of an angioma or that the vessels form the stroma for the cells. In these parts the bulk of the tissue is about equally vessels and cells. Between the cells there is no stroma. The cells are of several types (Fig. 4). For the most part they have a deeply staining spherical nucleus, often eccentrically placed. The protoplasm is quite abundant, and its

Fig. 3.— Section of tumor, showing its vascular structure and the relation of the tumor cells and vessels.

shape depends entirely upon the surroundings. Sometimes it is symmetrically disposed, and we find a large round or polygonal cell with a relatively small nucleus duplicating a large mononuclear leucocyte or a flat endothelial cell. Again, the protoplasm may be pressed out so that the cell tapers, shaped like a tadpole, with the nucleus at the head. The margin of the cells is always clear, and usually we find a space separating them.

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Many of the cells are multinuclear, even those that are quite small sometimes having two nuclei. The large multinuclear cells are of various types. The commonest form is about the size of the ordinary endothelial cell when viewed on the flat surface, and has from four to eight nuclei, which are usually near one end. Occasionally the nuclei are peripherally arranged, resembling a small, tuberculous giant cell, but this form is exceptional. The shape varies with the surroundings, but is generally polygonal. When the cells are cut across the nuclei are seen to lie in a mass upon each other, and it is demonstrated that these large cells are usually flat and of the general structure of endothelial cells. Cells are also

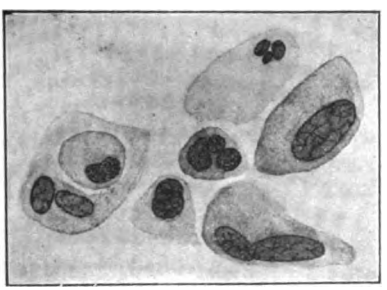

Fig. 4.—Different types of cells.

seen that seem to contain small cells within their protoplasm, resembling phagocytic endothelial cells as seen in lymph glands in the acute infectious diseases. Another type of the large cell has what at first sight appears to be a giant nucleus, but which is in reality a mass of nuclei, superimposed and apparently partly coalesced. A few cells, however, have a single enormous nucleus, staining intensely, very granular or ragged in structure. Probably such large cells as have just been described might be called mononuclear and multinuclear giant cells. Karyomitosis was not observed in a single instance.

As to the arrangement of the component parts of the

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tumor, the unit seems to be a blood vessel surrounded by a mass of tumor cells. Whether this vessel is very thin walled and with a large lumen, as is usually the case, or is covered by a thick mass of fibrous tissue, does not seem to influence the arrangement. Just outside of its connective tissue walls are always to be found the tumor cells, which are in contact with the connective tissue, but not united to or entangled in it, a distinct line of demarcation being present between the two structures as clearly as between an epithelial structure and its basement membrane. Between one vessel and its nearest neighbor lie only the cells, without any fibrous structure whatever. In other words, as before mentioned, the tumor cells may be considered as stroma holding the blood vessels in position or the blood vessels may be considered the stroma of the tumor. The only connective tissue demonstrable by Van Gieson's method is that about the walls of the vessels, or processes which occasionally branch from the larger vessels and the capsule, which run but short distances and seem to connect with vessels.

In the gross specimen calcified spicules were found. It is seen microscopically that these are not simple granules of calcium salts deposited in degenerated tissues, but true bone. None of them are large, and all are surrounded by a fibrous capsule. Within the calcified tissue the bone corpuscles with their branching projections into the canaliculi are plainly seen, most numerous just beneath the investing fibrous membrane. No other evidences of degeneration are found.

Just where to place this tumor as to classification is a matter of much interest. Primarily it must be considered a benign growth, as shown by its clinical history and its gross anatomy. It is evidently a vascular tumor, differing from the simple angiomas in possessing an intervascular matrix of cells of endothelial type. Borrmann[1] has classified the tumors of vascular origin in a

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way that seems especially clear and satisfactory as follows:

1. ANGIOMA.

Hæmangioma. Lymphangioma.

2. ENDOTHELIOMA.

Hæm(angio)-endothelioma. (No capillaries.)

Consists of vessels with a characteristic wall, which are filled with proliferated endothelium. Growth apparently not from new formation of vessels, but only through proliferation of the vessel-endothelium.

Lymph(angio)-endothelioma. (The common endothelioma of the literature.)

Consisting of cell-cylinders and cell-columns which lie in the lymph spaces. Growth by progression of the proliferating endothelium of the tissue spaces and lymph vessels along the course of the latter.

Capillary-endothelioma.

Consists of new-formed (tumor) capillaries, which arise from proliferated capillary-endothelium. The capillaries become filled finally by growing endothelium. Grows by newly formed capillaries which are protruded as fine tubes or cylinders.

3. PERITHELIOMA AND PERIENDOTHELIOMA.

Perithelioma.

Development unknown. Consists chiefly of many vessels with many-layered, superimposed, radially arranged cells, which lie perpendicularly on the outer wall of the vessels.

Periendothelioma.

Development unknown. Consists chiefly of many vessels with many-layered, superimposed, cells, arranged concentrically about the outer wall of the vessel, with their long axis in the direction of the vessels.

In the tumor under discussion it is found that the cellular portion always surrounds vessels, and is always the only structure between any two adjacent vessels. These cells do not seem to be in any way related to the endothelium lining the vessels, being always separated from them by a wall of connective tissue. Evidently they form for the vessels of the tumor a perithelial structure, for they lie outside of every vessel and form the tissue separating the vessels. As a perithelioma we recognize under Borrmann's classification a tumor whose cells are of the spindle-cell sarcoma type, arranged more or less radiating from the vessel they surround. Here, however, the cells are not of the ordinary sarcoma type, but are the flat cells which, with the exception of being multinuclear in many instances, resemble typical endothelial cells, even to the extent of sometimes acting as phagocytes for other smaller cells. The only cells in

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the adventitia from which such a tumor can arise are in the lymphatic sheath surrounding the vessel. Such tumors Borrmann calls periendothelioma, which is perhaps as exact and descriptive a name as any for such a growth. He states that in such tumors the cells are arranged parallel to the vessel wall, in contradistinction to the radial arrangement of the perithelioma or angiosarcoma. In this dural tumor no definite arrangement of the cells is seen; they seem to simply fill the spaces between vessels, and may be found cut in every direction in relation to the section of the vessel they surround.

Endothelioma of the dura mater is generally a benign tumor, less often malignant than when arising in the pleura and peritoneum, and still less so than endothelial tumors of the ovary and testicle.[2] It is especially the case that psammomas or sand-tumors are benign, and this tumor macroscopically might be classed as psammoma, although the number of calcific granules was smaller than usually are found in such growths. The calcareous infiltration in psammoma, however, is never an ossification, but simply a deposit in degenerated connective tissue (Sailer). Virchow[3] has recently defined his original use of the term "psammoma," and states vigorously that it does not include the endothelial tumors.

Giant cells have been occasionally recognized in endothelial tumors. Brosch[4] and Glockner[5] have both studied them. The latter describes both the mononuclear and multinuclear types seen in this case, and found them in four of sixteen endotheliomas of the pleura or peritoneum. He considers their origin to be the same as that of the small cells about them—that is, from the endothelium—and due to rapid division of the nucleus without division of the protoplasm. Others, he thinks, may form from direct segmentation and fragmentation of nuclei. The large uninuclear giant cells are probably the result of abnormal karyokinesis, and possibly

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also produced by fusion of a number of single nuclei. Sailer considers that in his case the multinuclear giant cells are apparently aggregations of cells, and many features of my own specimens suggest such an origin. In justice it must be said, however, that identical appearances would be produced by a division of the giant cells into smaller cells, and as a possible confirmation of this view is the much greater frequency of giant cells in the newest parts of the growth. Glockner considers it possible that the giant cells may undergo such a splitting up into small cells. One other source for the giant cells in this case must also be considered. The dura serves not only as a serous membrane, but as a periosteum for the skull, and any tumor arising from periosteum is, of course, especially likely to contain giant cells. In this connection may be recalled the ossified granules previously described. However, giant cells have also been found in endotheliomas not connected with bone—*e. g.*, the pleura, peritoneum, pulmonary vein.

In conclusion, this tumor may be stated to represent a benign growth of the dura mater, derived from the endothelium of the lymphatics of the perithelial layers of the blood vessels, the periendothelioma of Borrmann. As special structural features may be mentioned the presence of many uninuclear and multinuclear giant cells and spicules of true bone.

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January 14, 1901.

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REPORT OF A CASE OF EPIDEMIC CEREBRO-SPINAL MENINGITIS WITH SPECIMENS.

T. R. CROWDER.

The patient from whom this brain was taken was a Greek boy, 17 years of age. He entered the Presbyterian Hospital on the 6th day of April, 1900, and was assigned to the service of Dr. Billings. As no English-speaking friend accompanied the patient, no further history was obtained than that he had been in this country two weeks, had been sick one day and had a sister die of meningitis a year previously.

Examination on admission shows a well-developed and well-nourished boy in active delirium. The pupils are equal, moderately contracted and react to light. A small amount of coagulated blood surrounds the nostrils. No labial herpes or other eruption is present. The breathing is of the Cheyne-Stokes type. The lungs and heart are negative upon physical examination. The abdomen is retracted and soft. The patient persists in lying on the left side with the arms crossed over the chest. He resists all attempts to place him in other positions and when placed on the back the legs are straightened with difficulty. At once returns to left side when unrestrained. There is marked rigidity of the cervical muscles, but the head is not retracted. Kernig's sign is present. The eye grounds are normal. Temperature, 102.8 degrees F.; respiration, 26; pulse, 68.

April 7th: Temperature, 102 degrees F. to 104 F.; respiration, 20 to 28; pulse, 72 to 84. Urine: acid; sp.gr., 1028; a small amount of albumin; a few pus cells, cylindroids and hyalin casts are found by the microscope. The blood shows 13,300 leucocytes per

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c.mm. A puncture was made between the second and third lumbar vertebræ and an ounce of turbid fluid, containing small flocculent masses, was withdrawn. It contained pus cells and diplococci, a few of which were intracellular. In the afternoon a herpetic eruption is noticed on the lips, but no other eruption is present. The patient shades the eyes with the hands and groans as if in pain. The head is retracted and there is tenderness along the spine. The *tache cérébrale* is noted.

April 8th: Temperature, 101 F. to 103 F.; respiration, 20 to 36; pulse, 60 to 84. Involuntary urination marks the only change of condition.

April 9th: No change in the general condition. At 10:30 a. m. a second lumbar puncture obtains 1 c.cm. of thick yellow fluid. Many pus cells with many intracellular diplococci are found. Culture from the pus on agar-agar shows colonies of a diplococcus which destains by Gram's method.

April 10th: No change.

April 11th: 8 a. m.: Temperature, 101.6 F.; respiration, 36; pulse, 72. Blood: reds, 4,850,000; whites, 13,150; hemoglobin, 78 per cent. At 2 p. m. the temperature is 106.6 F., respiration 44 and pulse 164. There are repeated convulsions which begin by twitching at the right angle of the mouth, then the right side of the face and the right arm are involved and clonic contractions soon become general, and last approximately thirty seconds. During the intervals between convulsions the right side is entirely prolapsed and limp, while there is resistance in the left. The jaws are firmly set. There is some convergent strabismus. There are purpuric lines on the lower extremities, following the course of the superficial veins. Death occurred at 11:45 p. m., and autopsy was held eleven hours later.

ANATOMICAL DIAGNOSIS: Purulent lepto-meningitis; acute broncho-pneumonia; acute degenerative changes in the kidneys; acute degenerative changes in

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liver with areas of fatty infiltration; acute splenic tumor.

The body is that of a slender. moderately well-developed and well-nourished young man. Rigor mortis is well marked. There is lividity posteriorly; also some livid spots over the chest, cheek, arms and legs anteriorly. There is a dried herpetic eruption on the upper lip.

The abdominal cavity is empty; the peritoneum is smooth and shiny. There are no adhesions. The vermiform appedix points upward and inward; it is four inches long and two inches hang over the brim of the pelvis.

Both pleural cavities are empty; the pleura is smooth; there are no adhesions.

The pericardial cavity contains about two ounces of clear straw-colored fluid. The pericardium is smooth, without adhesions.

The tongue is normal.

The mucous membrane of the pharynx and esophagus is smooth throughout.

The thyroid gland is normal in appearance.

The mucous membrane of the trachea is smooth but the lower part is much congested.

The heart is of normal size. The external surface is smooth; both sides contain goose fat clots, extending into the great vessels. The endocardium is smooth and normal in appearance. The mitral orifice admits two fingers, the tricuspid four fingers. The myocardium is uniformly grayish-brown or red in color and firm in consistency.

The left lung is smooth externally; it crepitates throughout, except a few small circumscribed dark red areas on the posterior and lateral surfaces, which are slightly elevated; their diameter is from 1 to 2½ centimeters. The cut surface is reddish-gray and bloody, and on pressure yields a rather large amount of frothy

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fluid. Red areas corresponding to those on the external surface are indefinitely outlined in the substance, do not yield air on pressure, and are finely granular. The right lung corresponds in general both externally and on the cut surface to the left. On the posterior part are similar red areas of consolidation.

The liver is of normal size. Externally it is smooth, and dark bluish-red in color with lighter yellow mottling. A few areas are light yellow. The cut surface is grayish with yellow and red areas. The lobular markings are indistinct. Its surface is opaque and the substance rather soft.

The spleen is about three times the normal size. It is smooth externally. The capsule wrinkles easily and is bluish in color. The cut surface is dark red and the pulp rather soft.

The kidneys are of normal size; they cut with normal resistance; the capsule strips with slight resistance and leaves a smooth surface. The cortex is grayish and its markings are distinct. The glomeruli are visible. The cortex is one-third the thickness of the medulla. The mucous membrane of the pelvis is smooth.

The urinary bladder is distended with apparently normal urine. The mucous membrane is smooth.

The prostate is not enlarged. There are no changes in the seminal vesicles.

There are no changes in the scalp, skull or external surface of the dura, on the removal of which and exposure of the pia, there is noticed a yellowish exudate along the course of the vessels, occupying points in the sulci over the whole of the upper surface of the brain. These are much more noticeable on the left than on the right side. A large mass of semi-fluid purulent exudate occupies the spaces of the pia-arachnoid at the base of the brain, from the optic commissure back over the base and posterior part of the cerebellum; also in cleft between the cerebrum and cerebellum close to pedicles.

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A large quantity of thick yellow pus lies underneath the pia in the fissure dividing the lobes of the cerebellum.

The histological examination of the heart shows no changes. In the kidneys these changes are indicative of cloudy swelling. The liver is practically normal. The spleen shows no noticeable changes further than intense congestion.

Smears from the pus at the base of the brain show many cocci, which arrange themselves irregularly in groups or singly. They stain by Gram's method.

Smears from the subarachnoid fluid present many leucocytes, some of which contain cocci arranged in pairs. Cocci are also found free in the fluid.

Cultures from the pus show growths on the various media which are characteristic of the staphylococcus pyogenes aureus and albus. From the clearer fluid of the subarachnoid small translucent colonies develop on agar-agar plates which give growths in the media corresponding to the diplococcus intracellularis meningitidis. The cocci are usually arranged in pairs, sometimes in strings of four to six, and are destained by Gram's method.

Staphylococcus pyogenes aureus and albus are found in cultures from the heart's blood.

In cultures from the lung were found the staphylococcus aureus and albus and a Gram staining encapsulated, lanceolate-shaped diplococcus—the diplococcus pneumoniæ.

From the liver the staphylococcus pyogenes aureus and from the kidney the bacillus coli communis were cultivated.

The spleen gave no growth. In this case no point of entrance for the meningococcus was found. The just criticism is offered that the middle ears were not examined at the autopsy. From the anatomical findings it does not, however, seem probable that the inflammation was an extension in any direct manner from those

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cavities. The other organisms are to be looked upon as secondary infectious agents, in all probability terminal.

An interesting pathological fact is the association of a distinctly greater amount of exudate over the left cerebral hemisphere with the clinical finding of convulsions beginning on the right side and a right-sided paralysis between these convulsive seizures.

DR. WELLS.—Apropos of Dr. Crowder's remarks on meningococcus infections, I should like to make mention of a patient once in my care in the Cook County Hospital in the service of Dr. Herrick. It was a case of typhoid fever with onset marked by severe renal involvement, with an extremely small excretion of albumin and cast-ladened urine and much nausea and vomiting for the first week. During the second or third week an otitis media developed and perforated the tympanum spontaneously. Smears made from the pus showed the presence of an organism identical in morphology, situation, and staining characters with the diplococcus intracellularis of Weichselbaum. A pure culture was obtained and the cultural similarity was complete. Cultures made two days later yielded this same organism and the staphylococcus albus. Two days later only the staphylococcus could be found. There were never any meningeal symptoms. None of the clinical features of typhoid were wanting, Widal's reaction was present, and the bacillus typhosus was obtained from the urine and blood.

May 14, 1900.

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THROMBOSIS OF LEFT VERTEBRAL ARTERY AND ATHEROMA OF ARTERIES FORMING THE CIRCLE OF WILLIS, AND OF THE ANTERIOR, MIDDLE AND POSTERIOR CEREBRAL ARTERIES AND THEIR LARGER BRANCHES.

CHARLES A. PARKER.

The patient from whom this specimen was taken was a gentleman 75 years old, a bachelor, whose health had been excellent up to within three days of his death; his mental powers and physical endurance were commented on in the neighborhood as being noticeably above the average.

I was called to see him at noon, Sunday, December 31, 1899, and the following history was given: Two days before he had a moderate occipital headache and went to a physician, who gave him something for it, but it did not get better, although at no time was it severe. He went to bed Saturday night in apparent good health and spirits. At 3 a. m. he wandered downstairs and had to be led back to bed. Again at 8 a. m. he came down and said, "Good morning," but his speech was thick and he rambled in his talk so it was noticed that something was wrong.

When I was called he was lying down, but sat up with help when I examined him, and answered questions with yes or no fairly well, but did not attempt much more. Inquiry at a neighboring drug store developed the fact that he had left change on the counter two or three times recently, so that his attention had to be called to it, absent-mindedness.

Examination of urine proved negative as far as pathological finding, although his urine and feces were passed

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involuntarily. No evidence of trouble in other organs being found, the diagnosis of cerebral trouble was made, and, in the evening, the symptoms being more pronounced, cerebral thrombosis was considered the cause of the symptoms. Monday morning Dr. J. B. Herrick saw him in consultation and arrived at the same conclusion.

When examined by Dr. Herrick, Cheyne-Stokes respiration was quite pronounced, the pulse full and the aortic sound of the heart very distinct. His radial arteries were atheromatous.

Examination of nervous system showed delayed action of muscles of limbs and trunk, but no paralyses of any muscles were found and knee reflexes were normal. The pupils were small, the right slightly smaller than the left, but both responsive to light.

All the cranial nerves performed their functions properly, but consciousness was dulled from the first. The pulse varied between 56 and 90, and the temperature between 98° and 101°. The patient died Wednesday at 3 a. m. The brain was removed at 3 p. m. the same day and weighed 41 ounces and 5 drams. No peculiar changes were noted in the cortex, but in cutting the vertebral arteries in removal their toughness was quite apparent.

The base of the brain shows the left vertebral artery for 1¼ inches increased to double its normal size, while the cut end shows a very small lumen which is occupied by a recent clot which completely occludes it. The right vertebral artery shows similar changes with the absence of the clot so that a small lumen remains.

The walls of both arteries are yellowish white and stiff. The basilar artery has a milky appearance due to numerous atheromatous areas. The internal carotids are patent but sclerosed. The anterior, middle and posterior cerebrals, with their larger branches, show a similar milky appearance, but all appear to be patent; but a

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very interesting feature is the small size of the posterior communicating arteries, each less than a millimeter in diameter, with a lumen much smaller and still more reduced by sclerosis, thus preventing proper anastomosis of the internal carotid and post-cerebral arteries and consequent inevitable cerebral anemia and death, which would not necessarily have been the issue had they properly performed their function. The position of the thrombus and the help of the collateral circulation, although imperfect, explain the absence of localizing symptoms.

January 8, 1900.

THE CELLULAR CHANGES IN TUBERCULOUS MENINGITIS.—Dr. I. B. Diamond stated that plasma, lymphoid and phagocytic cells form the greater portion of the cell-infiltrations in the vascular and extravascular areas of the leptomeninx in acute tuberculous meningitis. The plasma and lymphoid cells emigrate largely from the lymph spaces of the arterial adventitia and from the finer capillaries. They proliferate largely by indirect division; a certain number, however, are derived from lymphoid cells. There are two kinds of phagocytes, 1, those which proliferate from the endothelial lining of the capillaries and lymph spaces, and 2. those from the subendothelial intimal connective tissue.

The most important of the vascular changes—the tuberculous endarteritis—develops in the following manner: Plasma and lymphoid cells accumulate underneath the endothelium of the intima; later the subendothelial intimal connective-tissue cells are found mixed with the former. They proliferate next to the elastic coat, are to a certain degree phagocytic and resemble epithelial cells. They also run together and form giant cells, and in this

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manner characteristic intimal tubercles develop. Changes of the endothelial lining of the arteries occur later, especially when there is caseation or hyaline degeneration of the collection underneath.

Of interest is the great production of plasma cells which is analogous to the cell changes described by Councilman in acute interstitial nephritis, while on the other hand, the production of phagocytic cells is analogous to the cell changes described by Mallory as occurring in typhoid fever.

May 13, 1901.

CELL DIVISION IN THE CENTRAL NERVOUS SYSTEM.—Alice Hamilton presented a paper dealing with cell division in the central nervous system of the white rat before and after birth; the number and distribution of the mitoses, the period up to which they persist, and their character. Mitoses were found along the ventricular surfaces in the early stages of development, gradually ceasing here, and increasing in the outer layers, until at birth, almost all are in the outer layers. At birth mitoses are numerous and persist up to the end of the fourth day; beyond this period no examination was made. The dividing cells are of two kinds; 1. small, devoid of visible cell body, resembling cells of the neuroglia; 2. large, with abundant cytoplasm, round, pear-shaped or spindle-shaped. These are in the gray matter of the cord and brain and correspond in measurements with the multipolar and pyramidal cells.

Conclusion: In the later stages of development the offspring of the germinal cells become partially differentiated, but without losing their power to divide. The large dividing cells are, then, immature nerve cells; the small are cells of the neuroglia. In the case of the white

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rat, these cells retain their power of division until after the fourth day of extra-uterine life.

June 10, 1901.

DANIEL N. EISENDRATH demonstrated specimens of brain abscess.

February 12, 1900.

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THE EYE.

THE GENESIS OF GLIOMA RETINÆ IN NEUROGLIA.

BROWN PUSEY.

It is commonly accepted by anatomists that the rod and cone cell layer of the retina is made up of highly differentiated cells, and this idea prevails notwithstanding differences of opinion as to their nature. Some authorities (Barker[1]) liken these cells to the so-called neuro-epithelial cells in the taste buds of the tongue; that is, they are thought to be differeniated epithelial cells with which the peripheral fibers of the bipolar cells come in contact. Another opinion, which is based especially on recent work by v. Lenhossek,[2] is that these cells are sensory nerve cells.

In any consideration of tumors of the retina one must remember that "histoid tumors (in which one or other tissue is more or less faithfully reproduced) are essentially benign; and malignancy and excessive cell proliferation (which is the essence of malignancy) go hand in hand with tumor formation of a pronounced embryonic type" (Adami[3]).

In recent publications Flexner[4] and Wintersteiner[5] have adopted[6] a different view. By independent investigations they concluded that the most malignant tumors of the retina are composed in large part of these most highly specialized cells. Wintersteiner's[7] description of the rosette figures found in such tumors is as follows: "Alle die rosetten und bandartigen oder bogenförmigen Zellenformationen als Aggregate von Stäbchen, event-

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uell Zapfenfasern aufzufassen. Die Zellkerne haben demnach die Bedeutung der Körner in der äusserer Körnerschichte; die glänzende, dem Lumen der Rosette respective der Concavität des Bogens zugewendete Linie entspricht der Membrana limitans externa, die kleinen Protoplasmaklümpchen welche derselbe anhaften, sind rudimentär entwickelte Stäbchen u. vielleicht auch Zapfen." Flexner's[8] description of the rosette formations is practically the same. From the study of these formations, Wintersteiner has suggested the term neuroepithelioma retinæ* to replace the term glioma retinæ. This suggestion has been the subject of not a little contention. In opposition it is urged that the rod and cone cell layer consists of cells intimately concerned with the visual sense, that, indeed, they are specialized nerve cells of a high order (v. Lenhossek[9]); and the position taken by practically all pathologists that nerve cells do not, at least in postnatal life, proliferate to form tumors.

In referring to primary tumors of the nervous system writers divide them into those arising from neuroglia and those composed wholly or in part of other elements of the nerve tissues. The latter group includes neuromas, consisting largely of nerve fibers, and gangliomas or neurogangliomas, i. e., tumors composed, at least in part, of nerve cells. Naturally, the questions that have arisen as to the proliferation of nerve cells in tumors have concerned the gangliomas (neuroma ganglionare). Concerning this class of tumors Birch-Hirschfeld[10] has written: "Für das Vorkommen ganglionar Neurome lassen sich nur vereinzelte und zum theil unsicherer Beobachtungen aufühen bei der Heterlopie grauer Hirn-substance, welche wiederholt durch den Befund grauer Inseln im Marklage des Gehirns erweisen wurde, handelt es sich um eine Entwickelungsstörung; der Aus-

*This term was used by Flexner with a question mark in his article describing such a tumor, published some months before Wintersteiner's first publication on this subject.

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gang wirklicher Geschwülstbildung von solchen Inseln ist nicht nochgeweisen." Gibson and Fleming,[11] in Allbutt's System, state that: "Ganglion cells have been found in one or two rare cases, but their occurrence is quite exceptional;" in Ziegler[12] we find that "probably all such formations must be regarded as the result of a disturbance of the embryological development of the brain;" "in all events, however, the investigations referred to are not sufficient to demonstrate certainly the existence of true neuromas of the spinal cord" (Lubarsch[13]). Casper[14] states that in animals true neuromas have not been demostrated with certainty. Klebs[15] dismisses the subject by saying: "In ganzen ist indess diese gangliosa Umwandlung der proliferenden Nervenfasern eine Seltenheit und besteht noch seltener ein solche Tumor Uberwiegend aus Neugebildeten ganglionzellen." Thoma[16] notices descriptions of such tumors by Klebs, Virchow and Wagner. Orth[17] cites two cases reported by Klebs and Soyka.

From the above quotations we see that Birch-Hirschfeld, Ziegler, Gibson and Fleming, Lubarsch, and Casper deny that tumors of the nervous system occur in which ganglion cells have multiplied to any considerable extent; Klebs finds that such tumors are rare; Thoma refers to three cases published in 1858, 1861 and 1863, and Orth notices reports of two cases.

The absence of evidences of proliferation of nerve cells in tumor growth is in accord with the results of investigations of the behavior of these cells in inflammatory processes. This subject has recently been very thoroughly considered by Tedeschi,[18] who reviews the literature and reports experiments of his own; he finds that cicatrices of more or less extensive cerebral wounds consist in greater part of neuroglia, in the center of which there are a few ganglion cells and a moderate mass of fibers.

In view of the inability of ordinary neurocytes to pro-

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liferate either in inflammatory processes or in tumors, it seems unlikely that the visual nerve cells of the retina (accepting the teaching of v. Lenhossek) should have that power.

There are yet other objections to Wintersteiner's views. One is the difficulty in accepting his explanation of the genesis of the rosette in the face of the fact that very similar formations occur in gliomas of the central nervous system. Another difficulty is encountered in the wall of the lumen around which the cells are aggregated to form the rosette. He considers this wall to be analogous with the membrana-limitans externa—a structure which all authorities agree is neuroglia. The lining of the channel in the rosette formations is within a mass of cells and is a part of a mass of cells which, according to Wintersteiner and Flexner, form embryonic rod and cone cells; it seems hardly probable that such cells should form a structure analogous to neuroglia.

Since Flexner's publications and preceding Wintersteiner's book, there appeared an article by Greef.[19] Using the silver method of Golgi-Cajal, with tissue from a tumor of the retina, he demonstrated that neuroglia cells formed the principal part of the tumor. His conclusion was confirmed by Hertel.[20]

In view of the conflicting opinions, I think that the publication of the results of the study of a specimen stained by Mallory's[21] neuroglia method may prove of interest.

The patient was referred to Dr. C. D. Wescott by Dr. F. C. Honnold; name, O. H.; girl; age, 4 years and 6 months. The parents are not in vigorous health The history of the family brings out the facts that three aunts of this child have squinted; the mother squints The patient's general physique is below par; the child is poorly nourished and very nervous. She has had the usual illnesses of childhood; in the last month has had

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capillary bronchitis. The eyes have always diverged; the parents have noticed this and also the fact that the child is "near-sighted," but they have not noticed any inflammatory symptoms. The left eye became red and painful two or three days ago, when the child was taken to see the family physician, who immediately referred it to Dr. Wescott.

May 13, 1899: P. C. Left eye. Eye on inspection seems rather smaller than a normal eye. Lacrymation, double injection, cornea clear, A.C. shallow, at angle of A.C. iris in contact with the cornea; A.C. clear; iris adherent to lens and pupil only slightly dilated by atropin; lens cloudy, and behind it in the vitreous chamber, by oblique illumination, an opaque body is seen. No red reflex. Eye tender. V. = 0. T. —1.

Right eye. Highly myopic—at least 8 D. Diagnosis given was guarded, but probably tumor. Ordered hot bathing, atropin and to return frequently for observation.

July 10, 1899: There has been less injection, but the condition now is about the same as when first seen. A.C. possibly more shallow. T. sub-normal. V. = 0. Probable diagnosis of tumor was made and enucleation advised.

January 10, 1900: Parents state that the eye has been quiet, but became red again a few days ago. Again advised enucleation.

January 12, 1900: Enucleation. January 17, 1900: Healing uneventful. May 22, 1901: The father writes that the child is in fair health

The eyeball, measuring 23 mm. sag., 22.5 horiz., 21.5 vertical diameter, was put immediately after enucleation in 4 per cent. solution of formalin in water, where it remained for forty-eight hours. Hardening was completed in alcohol. The eye was halved in its antero-posterior diameter, bisecting the optic nerve and cornea. One-half was embedded in celloidin and cut in serial sections. The sections varied from ten to twenty microns in thick-

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ness. Every fifth section was stained with hematoxylin-eosin; other sections were used for special stains—Mallory's neuroglia, Weigert's neuroglia, Weigert's fibrin and Weigert's elastic tissue stains, and stains for micro-organisms, etc.

Macroscopical Examination.—It is noteworthy that the eye is undersized. The sclera posteriorly is twice as thick as the normal tissue; A.C. shallow; iris bombe; lens cataractous posteriorly. The retina is detached and appears to be of normal thickness posteriorly, much thickened anteriorly and particularly where it is caught up and attached to the lens. The retina has streaks of pigment in it. The vitreous chamber is clear; the space between the retina and choroid contains some flaky opacities.

Microscopical Examination.*—The tissue of the cornea and sclera are histologically normal. The vessels at the cornea-scleral junction are distended. In the anterior chamber, along Descemet's membrane, which is normal, there is an albuminous deposit free from cellular elements. At the angle of the interior chamber the iris is adherent to the posterior surface of the cornea.

The iris shows the changes of an old iritis; it is thinned and made up of fibrous cicatricial tissue; adhesions exist between the capsule of the lens and iris at its pupillary margin. The ciliary body and ciliary processes show much fibrous cicatricial tissue, and the ciliary body contains an unusual number of pigmented cells.

The lens is cataractous. Under the anterior capsule, where the pupillary margin of the iris has become adherent to it, there are new connective tissue cells, which are mostly spindle shaped. The cortex of the lens is detached from the nucleus in a noticeable degree. The nucleus shows little change. The cells of the cortex show various stages of degeneration, many being swollen and granu-

* Drawings and a photomicrograph from sections of this specimen will appear in a coming number of the Journal of Experimental Medicine.

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lar, and there are many areas of calcareous deposits. In numerous sections the lens is seen to be invaded by strange cells which are pigmented, have a large granular nucleus, and are identical in appearance with the cells found in the retina. The fibers of the zonula are also infiltrated with similar cells.

The choroid is of normal thickness; the vessels are engorged with blood. At points it is the seat of an infiltration of large mono-nuclear and polymorpho-nuclear cells, a few plasma and mast cells.

The cells of the pigment layer of the retina show a most interesting increase in number. In some places they form rows several cells deep; in other places, considerable masses. One of these accumulations forms a detached mass, made up of pigmented cells from the pigment cell layer of the retina. This mass, in cross section in its thickest portion, is about 1 mm. in diameter; it runs through thirty sections, which average in thickness twenty microns. Therefore, it is about 6/10 of a mm. in its other diameter. This mass of cells is detached a little from the choroid, probably caused by shrinkage incident to the hardening. The cells of this mass have no regular shape—they are crowded together. The nuclei are large and granular, and the cell body is of varying size. The amount of pigment also varies.

In the optic nerve the cellular elements predominate over the fibers. These cells have large granular nuclei and but small bodies. There are some leucocytes.

Retina.—Posteriorly the retina is of about normal thickness, except just at the entrance of the optic nerve, where there is an increase of cells and a resulting thickening. Anteriorly there are several regions where the tissue is considerably increased in thickness, and near the ora serrata, in one series of sections, the retina is folded on itself. The lack of resemblance to normal retina is striking, the tissue having a reticular structure in which the fibers greatly predominate. Sections of the

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posterior part of this tissue, stained with Mallory's neuroglia stain, show that this portion is composed principally of a meshwork of neurogliar fibers. Scattered about are cells with large granular nuclei and unusually small protoplasmic bodies. The fibers are abundant; they extend in all directions. The fibers are long and narrow, and with Mallory's stain they are bluish-black. There are some cells which have the same large granular nuclei, but more of a protoplasmic body; and some of these cells contain pigment granules. These latter cells are found particularly along the inner surface of this tissue; in many places lying internal to the internal limiting membrane. The pigment is in granules and yellowish-brown.

Where the tissue is increased in thickness there is a resemblance to normal retina, and in this region the framework—the neuroglia tissue—takes Mallory's neuroglia stain well, and is seen to be excessive. The internal limiting membrane, or, speaking guardedly, the membrane in which Müller's fibers terminate, appears as a much thickened homogeneous layer. It is interesting to note that this membrane along its retinal surface gives the staining reaction of neuroglia; but in its greater extent along the internal surface it does not stain as such. Internal to the internal limiting membrane and in the cavity of the vitreous there are cells with large nuclei and protoplasmic bodies similar to those described above, and scattered among these cells one finds a few neuroglia fibers. The protoplasm of these cells in places contains pigment granules. In this region the fibers of Müller are increased and abnormally thickened. The most noticeable increase in Müller's fibers is in the region of the internal membrane and the fibers radiate from this region into the deeper layers of the retina. In the part of the retina normally occupied by the internal and external nuclear layers, in this thickened portion, there is a mass of fibers and cells.

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Near the ora serrata the tissue is folded on itself, the folding being particularly marked by the thickened internal limiting membrane. In this region the cellular elements predominate. The cells have large granular nuclei, and contain a moderate amount of cytoplasm. They are usually spindle-shaped. Some of the cells contain pigment granules. Interlaced around these cells are long neuroglia fibers, in some places very abundantly. Internal to the internal limiting membrane, and in the cavity of the vitreous, there is marked formation of new cells. In places the internal limiting membrane has been broken through by the cells. Interlaced among the cells are numerous long neuroglia fibers.

Many rosettes are scattered throughout this tissue. The formation of rosettes seems to be due to the tendency of the cells to arrange themselves in rows. In some places the rows are straight; in others curved and circular. either around a blood vessel or around an empty space.

The rosettes, as seen in sections stained by hematoxylin and eosin, are best described with Fuchs'[22] words as "resembling in the cross-section a tubular gland. Surrounding the lumen are long cylindrical cells, whose nuclei lie at their peripheral extremeties. The centrally directed extremities are bounded by a clear-cut line. From this latter short conical processes of protoplasm project into the lumen of the gland-like structure."

In sections stained with hematoxylin-eosin, perivascular rosettes appear to be made up of long cylindrical cells, whose layers of nuclei lie in the peripheral ends of the cells. The central ends of the cells appear to be lost on the wall of the vessel. The terminals of the filaments of the cells, ending on the blood vessel cause the wall of the vessel to appear thickened.

The appearance of both these forms of rosettes in sections stained with Mallory's neuroglia stain is very different from that when stained by hematoxylin-eosin.

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The neuroglia stain shows the layers of large granular nuclei; and, extending from the region of the nuclei towards the central lumen or vessel, are many long fibers, which give the staining reaction of neuroglia. Some of these fibers show an apparent attachment to the cell; others do not show any such intimate relationship. The terminal filaments of the neuroglia fibers, in part, appear to end in and form the wall; other fibers project into the lumen.

In a careful search through many sections I could find no cells that resembled rod and cone cells; a few large cells were found that might be taken for ganglion cells, such as occur normally in the nerve fiber layer of the retina. The blood vessels are rather plentiful. When terminal filaments of neuroglia fibers form a membrane along a vessel wall the latter appears much thickened. The membrane is homogeneous and hyaline and does not have the staining reaction of neuroglia. It is an interesting fact that the membrane found around such vessels stains with all stains as does the membrane corresponding to the internal limiting membrane. There are no signs in the retina of an inflammatory process, except near the optic nerve, where there are a few polymorphonuclear leucocytes around the blood vessels.

CONCLUSION.

The principal conclusion to be arrived at from the structure of this specimen is that this is a retina in which the neuroglia tissue has been developed at the expense, one may say, of the other tissues. In proof of this are the facts: (a) That the ordinary nervous tissue elements of the retina, the rod and cone cells, the layer of bipolar cells, the ganglion cells, are either absent entirely or present in very scanty numbers. (b) The neuroglia tissue is greatly increased, as shown by Mallory's stain.

Along the inner surface of the internal limiting membrane, and growing through it from the tissue outside, which in this eye represents altered retina, are cells with

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characteristic large granular nuclei and with varying amounts of cytoplasm, some of them containing pigment, and interlaced among these cells are long neuroglia fibers. In other words, neuroglia tissue has invaded the cavity of the vitreous. That these cells constitute a new growth is plain also from the fact that they have invaded and destroyed the crystalline lens. Composed as it is of neuroglia, the tumor is a glioma.

From the staining reaction with Mallory's neuroglia there seems to be no question of the neuroglia character of the rosettes. And, if these formations are compared with normal retinal tissue, as Flexner[23] and Wintersteiner[24] did, I think it would be more accurate to say that the wall of the lumen of the rosette corresponds to the internal limiting membrane (not the external); the radiating fibers, which are neuroglia fibers, to the fibers of Müller; and the distal nuclei to the neuroglia nuclei normally found in the internal granular layer. The projections into the lumen of the rosette are neuroglia fibers (not rudimentary rods and cones), which have not found their termination in the wall.

The rosettes being composed of neuroglia cells and fibers, the term neuro-epithelioma retinæ—as suggested by Flexner and Wintersteiner principally from their conception of the character of the cells in the rosettes—should not be accepted.

The results from the study of this specimen are in accord with what might be expected from a consideration of the facts spoken of in the fiirst part of this paper, and they certainly favor the retention for these retinal tumors of the term first suggested by Virchow and so long accepted—glioma retinæ.

There are good reasons for doubting the assertion of Weigert that the neuroglia fibers have no connection with the cell body. In these sections an intimate connection of the fiber with the cell could not always be discerned, but in some areas such a relationship was defin-

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itely demonstrated. This agrees with the observation made by Taylor,[25] who also used Mallory's stain, and with the conclusion of Bonome.[26] The last named author in a recent article states that "a characteristic quality, in which the neuroglia cells more nearly resemble the connective tissue elements, consists not only in the form of the cell body, but also in its relation to the fibrillæ, which in pathological conditions becomes more intimate than in the normal." This latter observation is in accord with Taylor's[27] suggestion of the existence of differentiated and undifferentiated neuroglia fibers in slowly growing tumors—a suggestion which seems very probable.

In the rosette pictured in figures IV, V, and VI, it will be noticed that in several fibers there are varicose formations. These are not nuclear figures, as is shown by the fact that the same varicosities are seen in specimens stained with hematoxylin and eosin, in which the varicosities show no disposition to take up the hematoxylin. Obersteiner[28] noted that changes in neuroglia fibers, of which varicose swelling of the processes is the commonest, may be observed in silver preparations, in alcoholic poisoning, uremia and other conditions.

The necrotic changes in glioma of the eye, which take place so frequently, in the cells a little removed from the blood vessels, are absent in this specimen. It is interesting to note that this eye was removed before there had been any plus tension in connection with the views of Greef,[29] who says that perhaps the peculiar structure of the retinal glioma is dependent on the fact that it is enclosed in the bulbus and that the tension soon becomes abnormally high; growth occurs with difficulty, and, as a result, the cells which do not lie immediately around the scanty vessels die and degenerate.

I did not succeed in staining sections of this tissue with Weigert's neuroglia stain. This was probably due to the manner of preparation of the tissue. Hertel,[30]

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in his case, also failed with Weigert's neuroglia stain. Wintersteiner[31] did not attempt to use Weigert's neuroglia method, because it was not available at the time he carried out his investigations. Recently normal retina has been satisfactorily stained by Weigert's method by Pines.[32] In the use of Mallory's neuroglia method I got the best results by differentiating with an alcoholic solution of ferric chloride after staining; Mallory advises this when good pictures of neuroglia fibers are desired.

The large mass of pigment cells described in the foregoing may be considered as a distinct tumor mass. Axenfeld,[33] reviewing the subject of retinal tumors and speaking of the growth of pigment epithelium, cites a case reported by de Vincenties, in which there was a formation of similar cells in a large mass, which was only differentiated from a tumor by degenerative changes. Axenfeld also cites Treacher Collins as having seen gland-like (drüsenartige) growths of the pigment epithelium, resembling a beginning tumor.

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TUBERCULOSIS OF THE IRIS.

WILLIAM H. WILDER.

Some difference of opinion seems to exist as to the frequency of this disease. Wagner (*Münch. Med. Wochenschr.*, 1891, Nos. 15, 16) states that 50 per cent. of all cases of iritis are of this character. Michel (Lehrbuch der Augenheilkunde) also regards it as very common, and says that forty or fifty of every hundred cases

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of iritis are tuberculous. Both authors seem to include in their category all cases of serous iritis in which there are small masses of exudate in or upon the iris, that simulate in any manner tuberculous nodules. Horner estimates that it will not be observed more frequently than once in four thousand cases of eye disease, while Hirschberg, of Berlin, saw only six cases of it among sixty thousand eye cases.

Velhagen (*Klin. Monatsbl. f. Augenh.*, xxxii, p 121) says that among eight thousand patients in the Eye Clinic at Göttingen, no case of tuberculous iritis was seen. With these latter opinions I think most ophthalmologists will agree, and we must conclude, therefore, that it is a very rare affection. Probably early observers who had opportunity for examining such cases considered them as either condylomata or sarcomata, or placed them in the category of idiopathic iritis; but with the invention of the ophthalmoscope and the discovery that tubercles develop in the choroid in connection with either general or meningeal tuberculosis, a more careful study of certain inflammations of the iris and ciliary body has determined their exact nature. Cohnheim demonstrated that tuberculous iritis can be caused by introducing particles from tuberculous lymphatic glands, granulations of tuberculous joints, etc., into the anterior chamber of the eye. More recently, investigators have caused the disease experimentally by injecting pure cultures of the tubercle bacilli into the aqueous chamber. The introduction of small masses of suspected tissue into the anterior chamber of the eye of a rabbit is employed as a means of determining whether such tissue is tuberculous. About twenty or thirty days after the injection into the eye, small, reddish-gray nodules make their appearance in the iris, and the eye becomes inflamed. The nodules increase in number, coalesce, and fill the anterior chamber with a mass of new tissue. The cornea becomes involved and the growth breaks

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through, thus destroying the eye. The animal usually dies from general tuberculosis.

Tuberculosis of the iris manifests itself in two forms:

First, Solitary Tubercle.

Second, Disseminated Tubercle.

The solitary growth affects one eye alone and develops as a small, round or oval nodule, usually at the periphery of the lower part of the iris. It is grayish-red in color and as it grows it fills the anterior chamber of the eye, and much resembles a neoplasm. Indeed, such a mass may easily be mistaken for a sarcoma. This also goes by the name of granuloma, a term, according to Fuchs, that was given by von Graefe "because Virchow, who made the anatomical examination of the tumor, designated it as granulation tissue." This term should be abandoned, for it is misleading, and liable to create confusion. As the growth increases, the cornea becomes involved and perforates, allowing the mass to break through, which presents as a pale yellowish or grayish mass similar in appearance to granulation tissue. It does not then continue to grow, but breaks down, and the eyeball gradually begins to shrink as the inflammatory process occasioned by the growth subsides. The eye is, of course, lost and phthisis bulbi ensues. General tuberculous infection may result.

In the disseminated form, which may occur in one or in both eyes, there are at first all the symptoms and signs of an iritis. Soon little yellowish-gray nodules surrounded by a slightly reddened zone, appear in the iris. These vary in size according to the stage of the growth but are from one to six mm. in diameter. Their favorite site is at the root or periphery of the iris, and they seem to be constantly changing, some disappearing while others are forming. Their predilection for the outer or root zone of the iris helps to distinguish them from the condylomatous nodules, so frequent in syphilitic iritis that usually are seen at the pupillary margin.

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Some of these tubercles may disappear completely leaving small patches of atrophied iris, while others may coalesce, forming larger tuberculous masses that fill in the angle of the anterior chamber.

The iris is dull and discolored, and flakes of lymph, and disintegrated tuberculous nodules may fill in and occlude the pupil. Firm and extensive adhesions form between the iris and the lens and the tension of the eye may become markedly increased. Lubrowski (*Archives Ophthalmology,* Vol. xxix, No. 3,) reports several cases in which glaucoma supervened. Ciliary injection is marked and the eye is often very sensitive to pressure. The ciliary body and choroid may be invaded, and even the cornea may be involved, the tubercles presenting the same general appearances in that structure as in the iris. As the case progresses, there may be bulging of the ciliary region and even perforation; or the process may subside with gradual shrinking and atrophy of the eyeball. Tubercular meningitis or general tuberculosis may supervene, so that the prognosis, both general and local, is bad.

Several observers, Leber (Bericht der xxi Versammlung d. Ophthalmol. Gesellsch., Heidelberg, 1891), Samelsohn (Bericht der xxiii Versammlung der Ophthalmolog. Gesellsch., Heidelberg, 1893), and Van Duyse (*Archiv d, Ophthalmologie,* xii, p. 478) describe a form of attenuated tuberculous iritis, presenting all the salient features of the disseminated form, which may end in spontaneous recovery, the functions of the eye being partly or wholly preserved. This form is slower in its course and affects older persons.

Both of the forms mentioned present the same histologic features, namely, the typical, tubercle formation around a central giant cell, but in milder forms of the disease, the bacilli are very scarce and difficult to find. It is assumed, therefore, that in some of these cases the exciting cause is not so much the direct action of the

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bacilli, as it is the irritation caused by the toxins generated by them, circulating through the delicate tissue of the iris, which, for some reason, is unusually sensitive and susceptible. This is a disease of childhood and adolescence, the large majority of such patients being under the age of twenty years. Of 121 cases reviewed by Schieck (Graefe's *Archiv für Ophthalmologie*, Bd. 50, part 2, 1900) ninety-six were under the age of 20 years; while of the remaining twenty-five, only six were over 30 years. The oldest was 55.

Most of the patients affected with tuberculous iritis have either pulmonary tuberculosis or tuberculous manifestations in other structures, such as joints, lymphatic glands or skin. Some have a bad family history, while a few have neither a family nor a personal history of tuberculosis, nor do they show any manifest signs of the disease, except the lesion of the eye. Such cases raise the very interesting and important question whether the iritis is primary or secondary to some other tuberculous lesion, and many capable observers take the view that it is primary. It is argued that the eye of a sound person may be infected locally through an abrasion of the cornea, or an ulcer of the cornea or conjunctiva, and that in such manner the bacilli may gain entrance to the deeper circulation of the eye.

January 14, 1901.

WELLER VAN HOOK demonstrated a carcinoma of the concha.

November 13, 1899.

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THE EAR.

VARIETIES OF CHOLESTEATOMA.

J. HOLINGER.

Between pathologists and otologists the following question was argued: Is it justifiable to use the same name (cholesteatoma) for two tumors, which are identical as to their macroscopical as well as microscopical appearance, but different as to their etiology?

1. Joh. Mueller and later Virchow described as pearl-tumor or cholesteatoma a rare tumor with the following characteristics: The size ranges up to that of a walnut. usually not over the size of a bean. It is well limited. The wall has the luster of a pearl and consists of epidermis-like tissue, or hornified cells. The contents have no blood vessels or nerves, but consist of scales or hornified or epidermized cells, which are arranged in layers, one around the other, like the shells of an onion. Between the shells are numerous crystals of cholesterin. The tumor occurs in various parts of the body, mainly on the base of the brain and in the testicle. It usually makes no symptoms, but is an accidental find at post-mortems. Most probably it originates from cast off particles of epidermis, and is therefore congenital and extremely rare. In his original publication of 1855, Virchow describes several cases of which we know *now,* that they were not congenital, but acquired.

2. Habermann, from clinical more. but also from pathological observation, described a tumor in the temporal bone, with the identical appearance. Many layers of epidermized scales, in onion shell-like arrangement. are surrounded by a capsule of pearl-like shining

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wall in the cupula of the tympanic cavity and the mastoid antrum, often filling parts or the whole process. It was connected through large holes in the drumhead, or even in the bone with the external meatus. Its wall continued without interruption to the lining of the tumor. Cholesterin crystals were present. This tumor was, however, not congenital, but had to be brought in connection with chronic inflammatory conditions of the middle ear and was acquired.

The careful study of the anatomy and pathology of the temporal bone by the otologists and the clinical observation left no doubt that this kind of cholesteatoma of the temporal bone is not a rare, but frequent finding, and is by no means an insignificant and good-natured growth like the congenital tumor of the brain and testicle, but causes quite often the death of its bearer by bringing the most infected material in contact with the lateral sinus, the dura and the pia, thus causing thrombophlebitis of the sinus, meningitis, or abscess of the brain. In order to understand this, we must remember two things; first, the epidermis, especially in children, has a great power of regeneration and shows this at all parts of the body where epidermis and mucous membrane meet. As soon as the mucous membrane is diseased, inflamed or otherwise impaired, the epidermis grows over it and covers the spot. In this way insulas or parts of normal epithelium are often overlapped and put out of existence. We find this at the nose, at the anus, etc. The process is especially energetic in the middle ear, as soon as epidermization has once begun. The aditus ad antrum, the antrum and the cells become inundated with epidermis. Afterwards this epidermis is under very unfavorable sanitary conditions. If in washing or in bathing any water gets in such a cavity through the opening of the drum, the water can not evaporate, but will keep up a certain amount of irritation, the epidermis forms more scales and one cast after

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another of the wall is cast off until the cavity is filled. But the process does not stop then, and here comes the second point. The cavity is enlarged by pressure and some authors think it even has a tendency for active enlargement. The bone septa between the mastoid cells are destroyed or absorbed. The bone can not resist in any direction. The luckiest occurrence is a perforation into the external canal or to the outside, and evacuation of the contents. Cases of that kind have been repeatedly observed, where an extremely slow-growing growth appeared behind the ear or in the neighborhood of the mastoid process on the neck. The diagnosis was difficult until the tumor burst and a big lump of dry scales was thrown out. This is, however, a most favorable though rare exception. The rule being the perforation towards the brain and death. The beginning of the whole usually dates back to the earliest childhood and is often brought in connection with one of those dreaded scarlet otitis. The organism adapts itself to the pressure and the slow growth may progress unnoticed for 20 to 50 years, even parts of the labyrinth may be destroyed before a meningitis or sinus thrombosis claims its victim at short notice after having carried around in the head a most perfect incubator loaded with germs for a lifetime.

So far I evaded the question how the epidermis entered into the middle ear. The study of this part of the subject is hardly less interesting than that of any of the rest. The simplest and beyond all doubt the most frequently used avenue is the one I have already hinted at, through a perforation of the posterior upper quadrant of the drumhead bordering on the annalus tympanicus with necrosis of a part of the adjoining bone. From there the way to the aditus ad antrum is measured by millimeters or fractions of millimeters only.

The second was under discussion for a long time, until Politzer settled it by showing a microscopical cut through a perforation of the drum, where epidermis of

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the outer surface continued without interruption over the edge of the perforation to the inner surface, where it had replaced the normal epithelium of the drum membrane.

Another road was described by Bezold as cholesteatoma of the drumhead or cholesteatoma of Shrapnell's membrane. In cases where the whole or parts of the drumhead, especially its most elastic part, which is Shrapnell's membrane, are retracted for years, as happens often in children with adenoids or in cases of adhesions of the drum to the promontory, sack-like excavations or diverticles will form. Now here two possibilities are given: Either the wall gets atrophic and the diverticle ruptures inward and its walls become adherent to the inner side of the drum and its surroundings in the middle ear, thus getting the epidermis to overlap the epithelium of the tympanic cavity. If the growth is once started it has no limit. The second possibility is that in this diverticle the scales accumulate and form a little cholesteatoma of Shrapnell's membrane. Cases of this kind have been described by Bezold. The tumors were only a few millimeters in diameter, but it is easily seen that nothing is in the way of a larger growth filling out the attic and the antrum.

You see, gentlemen, in the last two cases an inflammation or suppuration of the middle ear need not even have proceeded, and yet we have epidermis in the middle ear and cholesteatoma. This kind some authors claimed was congenital, until Bezold demonstrated specimens and pictures to prove their nature.

The investigations about cholesteatoma are far from being closed. In one of the last numbers of the "Archiv fuer Ohrenheilkunde" Habermann published several cases of cholesteatoma of the external meatus, where the external meatus contained cholesteatomatous masses the size of a pigeon's egg in an excavation of the meatus to the rear into the cells of the mastoid. Microscopical ex-

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amination of the wall of the diverticulum showed that the bone was not passive, but takes an active part in the process, inasmuch as it was changed from compact bone into spongy bone. Last January I showed in the German Medical Society of Chicago a patient with such an enlargement of the bony meatus, which was lined with a typical pearl-like shining cholesteatoma membrane, and from whom I removed masses the size of a hazelnut.

Much farther progressed was this same condition in a deaf and dumb boy of 12 whom I met at my examinations of the pupils of the institution for the education of the deaf and dumb in Jacksonville. The entrance to the meatus was normal, 1 cm. from the concha the meatus enlarged into a cavity the size of a walnut, lined with the well-known pearl-like membrane. The cholesteatoma, of which I show you a part, comprised the external meatus, the mastoid cells, the antrum, the middle ear and undoubtedly a part of the labyrinth. No trace of the drumhead or ossicles could be found. The wall was smooth and pearl-like, shining all over. That this process was inflammatory was shown by a sequestrum which was found in the center of the masses.

Finally, only one word as to the cholesterin. It was considered by Joh. Mueller as an ingredient part of the tumor. We know now that it is merely accidental and owes its existence to the decomposition of organic matter in an atmosphere where oxygen is lacking. Nevertheless, the name of the tumor is taken from its presence. To differentiate the two forms of tumors we call the rare one the congenital cholesteatoma, the other simply cholesteatoma.

Gentlemen, to show you that I did not occupy your time for a trifling matter, I simply state that by far the greatest number of so-called incurable chronic suppurations of the middle ear are due to epidermization of its lining and to cholesteatoma.

March 11, 1901.

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PATHOLOGY OF THE BONY FIXATION OF THE STIRRUP IN THE OVAL WINDOW. A NEW PATHOLOGIC PROCESS IN THE BONE (SPONGIFYING OF THE LABYRINTH).

J. HOLINGER.

The oldest writers knew that deafness is sometimes due to fixation of the stirrup in the oval window of the labyrinth, but not until the last few years has the real pathology of this process been known. It was my former teacher, Professor Siebenmann, in Basel, who brought the light into this darkness, by discovering and describing a new pathological process in the bony capsule of the labyrinth which never before had been observed and described.

Valsalva, about the middle of the last century, in a postmortem found the membrane of the oval window hardened to a bony substance, forming one mass with the oval window and the foot-plate of the stirrup. Twenty years later Morgagni made a similar observation. In 1777 Meckel said that fixation of the stirrup is a frequent cause of deafness. These facts were quite forgotten in the beginning of this century. Hyrtl, in 1845, first spoke again about them, however not in the human ear, but in whales; and Hagenbach (Basel) found it in other mammalia. Toynbee was the first man to approach this subject by describing 136 cases of bony fixation of the stirrup in the descriptive catalogue of his beautiful collection. Independently of him, Erhard in Berlin described the fixation, but entered more into the clinical importance of the matter. Twenty per cent. of all cases of deafness, he said in 1857, are due to the fixation of the stirrup. Voltolini and John Müller made experiments in order to explain these facts, but did not

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reach definite conclusions. During the last three or four decades all the well-known otologists of our days took part in these difficult investigations, viz., Troeltch, Politzer, Lucae, Moos, Schwartze. They all treated more the clinical side of the question. Schwartze first stated that the surrounding of the oval window seems to be a favorite place for new formations of bone, and that the nervous elements and labyrinth seem to be normal in this condition. A number of observations were published in the seventh and eighth decades of this century. Bezold in Munich (1885) read a paper about the first case where the diagnosis was made in the living and verified at the postmortem. Katz, in 1890, explained the conditions in question as a rheumatic arthritis; Habermann, in 1892, as an ostitis. Politzer, at the international medical congress in New York, published 16 cases of deafness due to a primary disease of the bony labyrinth which leads to ankylosis of the stirrup. Attention was repeatedly drawn to the fact that heredity is an important factor in this disease.

This is in a few words the development of this question up to the time Professor Siebenmann took a hand in it. His first objects of examination were a pair of temporal bones of a physician who for years was one of the editors of the *Correspbl. f. Schw. Aertze,* and who died of pneumonia at the age of 46 after having been deaf for more than 20 years. The membrana tympani and the middle ear were found normal in both ears. The mucous membrane was thin, transparent and attached tightly to the bone. The temporal bone contained a great many air cells. The niches of both the oval and of the round windows were flattened and narrow. In trying to move the stirrup it was found that it was immovable in both ears, which was proved beyond a doubt when a fine probe was stuck into the head of the stapes and moved. The left temporal bone was macerated, the right one prepared for microscopical cuts.

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The left, the mascerated temporal bone, showed the following condition: The surface was rough, probably from the decalcifying action of Müller's fluid, in which the bones laid for several years. The round window was normal. The oval window, in which the stapes remained ankylosed, notwithstanding the above said action of Müller's fluid and the maceration, was narrower than the normal, so that between the branches of the stirrup and the walls of the niche, a very narrow slit was left. The walls on both sides showed impressions of the branches of the stirrup. On the rear branch of the stirrup it looked as if the foot-plate and the branch had formed a resistance against the growth of the bone, because on both sides the bone protruded considerably without entirely surrounding the branch, partially embedded in the new bone; much the same effect as when one presses the hand into a soft pillow. To get a view from the inside a cut was made through the labyrinth. The inner side of the frame of the round window was normal. The oval window showed a broad flat thickening all around. This thickening increased gradually from all sides towards the stapes and stopped in a ring-like margin or edge around the foot-plate, without overlapping it. The rear end of the foot-plate was not in its normal position; it protruded into the vestibulum and therefore was cut away by the saw. The cut surface is round, and with a magnifying glass one can see that the foot-plate and the frame of the window form one continuous spongy mass. The new formation of bone seems to be entirely confined to the surroundings of the oval window. None is found in other parts of the labyrinth. The right middle and inner ears were prepared for microscopic examination. It is not necessary to give all the details of this process, which lasts over three months. Sixty-seven cuts of 50 u. were made and stained in picrocarmin and hematoxylin. The bony tissue in the neighborhood of the cochlea and vestibulum seems to

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be a fine spongy mass and is more intensely colored by carmin. The eighth cut strikes the beginning of the oval window. There is no trace left of the membrana fenestræ ovalis, but the foot-plate forms one mass of bone with the frame of the window. The line of demarcation between the two has disappeared. The foot-plate seems to be thickened around its margin. On the rear part of the circumference a small area of connective tissue seems to be left. Only one cut, which goes through the insertion of both branches of the stirrup, shows the foot-plate in its normal thickness. The rest forms one spongy mass with the surroundings. An exostosis even extends across the whole foot-plate. The stirrup is not in its normal position. It seems to be luxated. The anterior circumference of the stirrup seems to be lifted out of the window and protrudes more towards the middle ear, the posterior part is pushed inwards towards the vestibulum. The stirrup does not fit in the oval window like a window in a frame, but rather seems to be swung upon pivots which are situated in the middle of the long sides of the foot-plate. The lower parts of both branches of the stirrup, the foot-plate and the frame form one spongy mass of 0.5 mm. in thickness. The spongy bone is colored intensely red with carmin, and this color spreads in the capsule of the labyrinth up to the tensor tympani muscle. The part of the cochlea which borders on the middle ear shows the greatest extension of the changes. The posterior part of the capsula is normal. The capsula, the middle convolution and the spindula of the first convolution are equally affected. A few small strips of the cochlea are left normal. New formed but not spongy bone of normal coloring qualities and lamellar structure is found in the spindula. It is perforated with narrow Haver's canals with cartilaginous walls. The contents of the gangliar canal show a great many round cells. The canals for the blood vessels and nerves have abnormally many branches and many spindle-shaped

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thickenings, thus showing a knotty appearance. On the cupula there is a zone which is less spongy, but contains a great number of blood vessels and cells and some giant cells. The open spaces between the spongy network are filled with connective tissue, containing few nuclei and few blood vessels. The spongy bone is sharply differentiated from the normal. The frame of the round window, too, is changed, and an exotosis overlaps its membrane. The Corti's organ is normal, and so is the epithelium of the macula utriculi. The stem of the acoustic nerve shows nothing abnormal. The periosteal connective tissue of the canals for the nerves and blood vessels is very tense and has a yellow pigment. The posterior spiral vein is narrower and its bony canal is filled with connective tissue. The number of the ganglia and nerves is not less than normal, but their diameter is smaller.

The tensor tympani muscle is normal, but the stapedius muscle consists of connective tissue.

Stating in a few words all the described changes: The pelvis ovalis of the left ear is narrower than normal. The lig. annulare is totally ossified. A spongy wall of bone is formed around the vestibular side of the oval window. The posterior part of the stapes is moved inward, the anterior outward from its normal position. On the right side there are similar conditions with the only difference that the upper part of the lig. annulare is not entirely replaced by bone. The process of the disease extends over a great part of the bony capsula of the cochlea. The spindula consists of bone, which decreases the lumen of the canals of the nerves and the blood vessels. The microscopic examination shows, furthermore, an increase of the perivascular and perineural tissue. The stapedius muscle is completely degenerated, and the luxated position of the stirrup is identical with one produced by the action of the stapedius muscle. The question arises whether or not there is a certain connection

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between those two conditions. Which is cause and which is effect, must be left to clinical experience.

The second case was that of a patient who underwent severe bodily exertions during the Civil war, and since that time became gradually deaf. He never complained about pain or dizziness. The right temporal bone showed the following conditions: External ear, drumhead and middle ear were normal. The upper and anterior part adjacent to the oval window was found diseased. The diseased part reaches nearly to the facial nerve and to the tensor tympani muscle. A small bridge of 0.2 mm. divides it from these organs. Anteriorly it extends to the nerve utriculo-ampullaris. It penetrates here the whole thickness of the capsula of the labyrinth and lies directly underneath the endosteum of the vestibulum. The focus of the disease occupies the whole upper part of the niche of the oval window. The membrane of the oval window. the lig. annulare, is changed into a small zone of connective tissue, which contains small parts of osteoid tissue. The foot-plate of the stirrup is from five to ten times its normal thickness at different parts. This fact is probably responsible for the narrowness of the ligament in its lower part. The mucous membrane of the drum cavity is very much thicker over the diseased parts. An exostosis of the frame of 0.045 mm. does not and another one of 0.2 mm. in width does reach the foot-plate. Another similar bony bridge over the much changed lig. annulare is found in the upper margin of the middle of the foot-plate. The focus reaches upwards to the facial nerve and for a distance of nearly 1 mm. forms the wall of the canal. The foot-plate as well as the frame of the window has irregular protuberances of bone into the lig. annulare and the mucous membrane of the niche. The branches of the stirrup are normal, and so are the rest of the cochlea and the semicircular canals.

About some finer details an opinion was gotten from

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Dr. Hanau, a pathologist who did much work in pathology of the bones. Normal parts were always kept at hand for comparison. In those parts which may be recognized as diseased, the bone corpuscles are more numerous and larger than in the normal. The boundary of the bone towards the mucous membrane of the drum cavity is irregularly concave and convex, at parts almost like Howship's lacunæ, but without giant cells. The diseased bone is thicker than the normal, from 2 to 10 times its size. The Haver's canals are wider and more numerous and often communicate. There are a number of cavities filled with marrow and connective tissue with few nuclei. A pretty large number of Howship's lacunæ are found. The bone corpuscles are more numerous, irregularly distributed, large and clumsy, similar to newly formed metaplastic bone. The limit between the normal temporal bone and the diseased bone is sharp. The bridge from the frame to the foot-plate has especially large and irregular corpuscles.

The left temporal bone shows no change whatever about the semicircular canals. The interior branch of the stirrup disappears to more than two-thirds of its length in the much thickened foot-plate. A small space is left between the branch and the wall of the niche, which even is bridged over. All around the frame of the window are many cavities of marrow, containing connective tissue. At one spot the focus reaches the tendon of the tensor muscle; at another the lig. spirale. The posterior branch of the stirrup is thick and together with the foot-plate is pushed outwards. The rest of the labyrinth is normal in all its parts. There are two bony connections between the frame of the oval window and the foot-plate. The rear one is 0.75 mm. in length, the other one is in the middle between the anterior and posterior margin and is 0.95 mm. in length. Two other bony adhesions are on the lower margin of 1.25 mm. and 0.65 mm. in length. The focus reaches with one arm to

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the cochlea and forms its base. A great number of bony protuberances from the foot-plate as well as from the frame enter into the remnants of the lig. annulare and touch each other without perfectly uniting. A big exostosis protrudes into the niche of the oval window. The mucous membrane of the drum cavity is considerably thickened; in the attic where the bone is not changed it is normal. The bone of the frame is porous. The pores are cylindrical, and contain connective tissue with few nuclei. Wherever there is ankylosis there is no cartilage and where the cartilage is left its structure is changed.

As in the first case, the disease is not confined to the oval window, but has progressed as far as the cochlea. The bone corpuscles were found large and clumsy and more numerous than in the normal. All these facts point to new formation of bone. We can not define this bone as a simple change of the normal, but it must be considered as new formed metaplastic bone emerging from connective tissue. This opinion was pronounced by Dr. Hanau and Professor Roth, my former teacher of pathology.

In by far the greatest number of these cases the pathological process is found on both sides. A simple incrustation of the lig. annulare with lime salts has been described, but must be rare. Other cases were found where ankylosis occurred through hyperostosis of the niche alone, connecting it with a branch of the stirrup without the lig. annulare being involved. The process is usually confined to the surroundings of the oval window. The ankylosis formerly was considered as being a consequence of chronic catarrh of the mucous membrane of the tympanic cavity. But there are many cases where there is no trace of a preceding inflammation. Other authors, Moos, Schwartze, Habermann, thought that the periosteum was the cause. This was refuted by Politzer and Bezold. This question can not be considered a settled one. Hanau and Bezold agree that it is

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new formed metaplastic bone, originating from connective tissue. Toynbee saw cases that he classed as rheumatic or gouty, and so did Katz in 1890. But more resemblance might be found with arthritis deformans. Yet no proof can be given for either one of these views.

During my visit last summer, Prof. Siebenmann spent several afternoons in carefully showing and explaining to me his very many specimens on this subject. The disease never leading to death, it must be called a matter of good luck that specimens are obtained from patients on whom the diagnosis was made during life. The chances are so much smaller in this country, where patients change their attendants and hospitals almost with each new illness. Therefore, we have to rely upon what information we get from abroad. I know the sharp critical nature of the investigator and the years of careful work that he has spent, so I am sure that these results are reliable. Specimens have been promised to me which I shall not fail to show you as soon as they arrive. The first experiences of Prof. Siebenmann were published in a dissertation of Dr. Hartmann which reappeared in the Z. f. O. from which I took the above data. A new light was thrown on the subject by an experience which Siebenmann published in the same periodical (Vol. xxxiv, 4) under the heading "Multiple Spongy Patches in the Capsule of the Labyrinth, as a Finding in a Case of Progressive Deafness."

It concerns a lady of 52 years who died of ulcerative endocarditis with miliary abscesses in the pia, the brain, the kidneys, the submucosa of the stomach and intestines, in the thyroid and parotid, embolic infarcts and hemorrhages in the kidneys, spleen, larynx and trachea. It is easily seen that these are all conditions which can not have the least bearing on what was found in the two labyrinths, which showed the most remarkable changes. In both organs several spongy patches were found in the bony capsula of the semicircular canals, of the vestibu-

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lum and the cochlea. Osteophytes were found on the tympanal and vestibular surface of the frame of the oval window. The cartilage of the stapes and the lig. annulare had begun to ossify. The ankylosis of the stirrup, therefore, was incomplete, but the same process which would have led to ankylosis was found attacking quite a number of parts which so far always have been found free. In the right labyrinth six foci of the same character in the left four were found. On the right side two and on the left three foci were confined to the semicircular canals. Only two foci of the right labyrinth are connected with each other by small bridges of diseased bone, all the others are circumscribed and independent.

The specimens, furthermore, allow us to form an idea about different stages of development, of the formation of the spongy parts and the starting point of each focus. I should like very much to describe all the minute details of this process, but I am afraid to take up too much time. Resorption and new formations occur simultaneously. They begin around the Haver's canals, on the side toward the labyrinth. Multinuclear giant cells can often be found. Clumsy irregular bone corpuscles are formed with numerous, clearly visible projections and one to two nuclei. The Haver's canals and the Haver's spaces are not alone changed, but all interglobular spaces which contain cartilage are replaced by new-formed bone. The cartilaginous layers of the oval window and stirrup are absorbed and replaced by bone in connection with large vessels parting from the bone. Later on, the bone takes a lamellar structure, the bone corpuscles become concentrically arranged, and the nucleus shrinks. The spaces of marrow are formed by replacing cells and blood vessels with connective tissue.

The origin of this whole process was found by careful comparison with other bones. It was not in the peri-

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osteum as Bezold suspected, nor in the capsule of the labyrinth as Politzer thought; but the oldest parts were on the limits between the primary capsula of the labyrinth which was formed by the endochondrium and the secondary bony capsula originating from the connective tissue of the periosteum.

The spongy spaces never were so large that we might call the process a real osteoporotic one, because there is much new formation of bone. The resorption is best marked in the neighborhood of the large canals for the nerves and underneath the endosteum of the labyrinth, so that in there the endolymphatic fluid is at some places separated only by a thin septum of connective tissue from the large lymph spaces of the spongy area. Large perivascular spaces connect the labyrinth with the porus acusticus and the tympanic cavity.

Why the capsula of the labyrinth shows such changes from its normal eburneous texture to spongy bone is a question which Siebenmann tries to answer. The labyrinth of the new born has the size of the adult. The capsula, although as hard as ivory, often contains islands of primary cartilage, which are most often situated near the large spaces of the labyrinth, and can be seen at times even with the naked eye, on cuts which are colored with eosin hematoxylin. These islands are found most often in the neighborhod of the posterior half of the oval window, and in the lowest parts of the cochlea. In one case even a piece of cartilage as large as a hempseed was found. The origin of this process must be attributed to the change of this cartilage into compact bone. The contents of this spongy bone are fibrillar marrow (Fasermark).

We must consider these works of Siebenmann as the beginning of a pathology of the labyrinth, which so far was confined to a few discriptions of perforative suppurations and penetrating fractures.

December 11, 1899.

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RESPIRATORY SYSTEM.

PRIMARY CARCINOMA OF THE LUNG.

E. R. LE COUNT.

The following case occurred in the St. Elizabeth Hospital in the service of Dr. Kramps, to whose courtesy I am indebted for the following notes from the clinical history:

Clinical History (Abstract).—Mrs. K., housewife, was taken ill 18 months before entrance into the hospital, which occurred August 12, 1899. Her health has always been good. The illness began with taking cold and cough has been present with periods of exacerbation ever since. The expectoration has often been bloody and frothy; examinations for tubercle bacilli on several occasions were negative. The material examined was, as a rule, very viscid and gelatinous. Pain in the chest was more constant and lancinating in character during the early part of the illness. At the time of entrance she complained of some pain in the chest, difficulty in breathing, and a troublesome cough. Examination showed considerable emaciation; skin yellowish and dry; labored respiration of the abdominal type; bulging thoracic arch and prominent intercostal spaces. On auscultation large, coarse râles were heard over both lungs, bronchial breathing over the upper part of the left lung, a flat percussion note over the same area and normal physical signs over the lower part of both lungs. Death, which occurred December 17th, was preceded by emaciation and increasing dyspnea. The clinical diagnosis was pulmonary tuberculosis.

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Abstract of the Necropsy Record (20 hours after death).—Anatomic diagnosis: primary carcinoma of the lungs, adhesive pleuritis, atheroma of the aorta, coronary and cerebral arteries, hypertrophy of the heart, chronic mitral and aortic endocarditis, passive hyperemia of the liver and kidneys, senile atrophy of the spleen and ovaries, "corset" liver, cholelithiasis.

The heart weighs 300 gms. The posterior mitral valve and attached borders of all the cusps at the aortic valve are the seat of considerable calcific deposit. The cavity of the left auricle appears large; the wall of the left ventricle averages 13 to 15 mm. in thickness. The right ventricular wall measures 5 to 7 mm. In some places the walls of the coronary arteries are found to be entirely surrounded with firm calcified plates.

The right lung weighs 800 gms., and is consolidated throughout the upper and middle lobes; there are also rounded small districts that feel firm in the lower lobe. The pleura, covered with torn and ragged broken adhesions, is dark from coal pigmentation. The pleura over the upper lobe is edematous as though an exudate had been coagulated beneath it; this is uniformly gray and soft and resembles the cloudy meningeal hydrostatic edema that is often encountered. There are numerous puckered scars in the pleura and often the two pleuræ are adherent at such places. The anterior margin and diaphragmatic surface are emphysematous, pale and inelastic. In the upper lobe there is found on section a cavity 2.2 cm. in diameter; it has smooth walls formed by a firm gray tissue in which there are patches of coal pigment; it contains a dirty gray, slimy fluid. It does not communicate with any other cavity, nor with any of the larger air passages. In the lower part of the upper lobe are similar smaller cavities, also one in the lower part of the middle lobe. The bronchi contain a grayish pink, thin mucus plentifully mixed with air.

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The bronchial walls are smooth and light pink in color. The lining of the small bronchioles is ecchymotic.

The left lung weighs 650 gms. Externally there is marked anthracosis; along the internal border, next to the vertebræ, it forms a continuous patch 7.5x1.5 cm. Near the apex of the upper lobe is a drawn and puckered scar 0.5 cm. in depth; a similar scar occurs on the outer border and several smaller ones on the remaining external surface and the diaphragmatic surface. Beneath the scars are felt nodules of consolidation. There are also some regions of consolidation felt which are marked externally by elevations of the pleura and the pleura itself is grayish white and thickened. In the upper lobe the consolidation is diffuse and occupies the upper and posterior two-thirds of the lung. On section the consolidated districts show a greenish-gray surface mottled with patches of coal pigment, with pin-point white spots and slightly larger yellowish gray spots which are miliary and submiliary in size. In the upper lobe where the consolidation is diffuse, there occur cavities with smooth walls, containing a turbid, slimy fluid. The largest of these would contain a pigeon's egg. The cavities are irregular in shape; they communicate with one another and in their walls and in the adjacent tissues the white points are no more numerous than in regions where there are no cavities. The cavities are mostly in the apex and close to the pleura. Cross sections of the nodules felt beneath the puckered scars in the pleura, show the same greenish-gray consolidation, the granular surface and a pigmented center. The edges have a scalloped outline.

There were no tumors found elsewhere in the body.

Bacteriologic: Smear preparations made from the small white points and stained in various ways showed long-drawn out threads which were at first supposed to be streptothrices; but later developments disproved this supposition. No bacteria were found. Inoculations

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upon tubes of agar, glycerin agar, and blood serum were made with the material from the white points with the result that pure cultures of a streptococcus were obtained. Death of a full-grown rabbit was brought about in 24 hours by carefully inserting some of the white masses into the abdominal cavity; and smear preparations from the peritoneum showed only a streptococcus which stained by Gram's stain. Plates made from the peritoneal exudate showed this streptococcus in pure culture.

Histologic: A section taken from the region of diffuse consolidation is made up of islands of epithelial cells which often contain masses of eosin staining necrotic tissue in their central portions. These islands are separated from each other by delicate bands of connective tissue which resemble the alveolar walls and also by large blood vessels around which there is usually a marked deposit of coal pigment. In this section no bronchi can be found, but around some of the large arteries there are channels filled with tumor cells. These channels are large, as large as the accompanying arteries, circular in form and possess thin walls; the tumor cells which fill them are usually necrotic in the central parts so that a circular eosin staining center is entirely surrounded by a zone of epithelial cells. The tumor cells are large cells which often contain nuclear figures. The cells vary greatly in size and appearance and have no characteristic grouping. It is at once noticeable that the clusters which these cells form are fairly uniform in size and of such a size as would be produced by filling the air chambers. The tumor cells of any one cluster are always in contact. A section which includes the edge of a cavity shows no tendency to a wall formation; a zone of leucocytes with greatly fragmented nuclei line the cavity and immediately outside, the transition to tumor tissue such as is found elsewhere in the diffusely infiltrated tissue is very abrupt. All

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regions adjacent to the cavity are very inflammatory. The diffuse infiltration around a large bronchus presents no characteristics which differ from those present in similar districts elsewhere. In a cross section of a large bronchus elsewhere, there is an entire absence of the lining epithelium and in its place and impinging on the lumen is a very cellular tissue with newly formed blood vessels. The cells are such as occur in granulation tissue and among these are many plasma cells. The mucous glands lying deeply within the wall close to the plates of cartilage are infiltrated with the cells of this granulation tissue to a marked degree. In the superficial parts of the granulation tissue close to the channels are many tumor cells similar in all respects to those present elsewhere. Where the pleura appeared edematous anatomically, there was found microscopically a marked cellular exudate which had undergone considerable organization. Sections from a small nodule in the left lower lobe show adjacent to a cross section of one of the branches of the pulmonary artery, two large channels with thin walls which are filled with tumor cells. The centers of these cellular plugs have undergone necrosis. From their situation and size one is forced to the conclusion that these are branches of a pulmonary vein. In sections from a nodule in the right lower lobe a similar condition was found. The nodules in the lower lobes show the process of invasion of the lung tissue by the tumor cells very nicely; often alveoli only partly filled with epithelial cells are found at the edges of the nodule, or others more completely filled.

April 9, 1900.

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REPORT OF A CASE OF SYPHILIS OF THE LUNG, WITH FURTHER CONSIDERATION OF THE SUBJECT.

W. A. EVANS.

Patient, L. H., was an inmate of Alexian Brothers' Hospital in the service of Dr. J. H. Hoelscher, attending physician, and Dr. Julius Hess, interne, during May and June, 1899.

Family History.—Father died of strangulated hernia. Mother died of old age—88 years. Three sisters and two brothers living. One brother died during infancy. No history of tuberculosis or carcinoma.

Personal History.—Drinks moderately. Married and is the father of twelve children. Eight are living. One was burned to death, one died of an exanthematous disease, one died at seven months, one died of diphtheria. He is now 54 years of age.

Past Illnesses.—Ordinary diseases of childhood. Denies any venereal history. Quotidian malaria at 33 and 35.

Present Illness.—In November, 1897, took cold and was confined to bed for some weeks. During first two weeks expectorated mucus mixed with blood and black particles. Edematous in eyelids and feet, especially in the morning.

April 1, 1898. Had great pain in left side of chest. Two weeks later chest was aspirated and one quart of dark-red, offensive fluid was removed. One quart was removed April 25, June 16, July 4, and July 9. Entered hospital July 19, 1898. Was tapped July 20, 29, and August 17. About one quart of bloody fluid removed at each tapping. Discharged August 24. Tapped by family doctor eight times, between September, 1898, and April, 1899.

Re-entered hospital May, 1899.

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GROSS ANATOMY OF LUNG AND TESTICLES.

Considerable number of pleuritic adhesions, which are comparatively old and firm. There is no general pleural thickening; in fact, there is no pleural thickening away from these bands of adhesions. The lung does not completely collapse. There are multiple nodules which can be felt in lung substance. Some of these are comparatively near the pleura. The lung "cuts" tough. Multiple nodules are found of all sizes up to 2 cm. in diameter. The location of these is in the middle segment of the lung, and rather regardless of lobar distinctions. They are rather more numerous near the root of the lung than toward the periphery. The largest of them are composed of a central necrotic mass. This mass is a light gray, almost pearl, in color, dry and crumbly. Around this is a clear-cut wall presenting a hyaline glistening appearance. Still further removed from the center there is consolidation from solid connective tissue growth, or from the contraction of fibrous tissue. There is no evidence of an adjacent exudative pneumonia. Still more peripherally there are zones of emphysema. The smaller nodules seem to have the same structure. The lung is the seat of a diffuse interstitial pneumonia. The peribronchial connective tissues are markedly thickened. There is no *great* thickening in the alveolar walls. In the peribronchial lymph glands of the base one sees the same gummatous masses, to-wit: A dry, caseating crumbly central zone, surrounded by a firm hyaline-appearing capsule.

Right Testicle: The right testicle is decreased in size, firm in consistency and "cuts" tough. The organ is very pale white and surrounded by a dense, thick, heavy, fibrous capsule. In the center some parenchyma can be demonstrated. This parenchyma is as thick as the capsule. Bands of interstitial tissue can be seen running from the capsule into the parenchyma. No distinction

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can be made between tunica albuginea and the tunica vaginalis.

Left Testicle: Decreased in size. Increased in consistency. "Cuts" tough. There is no distinction between albuginea and vaginalis. A large quantity of fibrous tissue is seen running from tunic to the interior. There are multiple gummatous masses in parenchyma of the organ. The largest of these measure 1 cm. in diameter. These are yellowish in appearance. They are not necrotic in appearance. They are surrounded by a capsule that looks hyaline.

Microscopical Examination.—Sections were made from the testicles, from larger and smaller gummata, and from the areas of interstitial pneumonia. Some of these sections were stained with Ehrlich's stain for tubercle bacilli. Results were negative. Staining was done for syphilis bacilli according to method of Van Niessen, with negative results. Other sections were stained with hematoxylin and eosin, Van Gieson, Weigert's stain for elastic tissue; Unna's orcein stain for connective tissue. Unna's stain for hyaline and colloid; methylene violet and oxalic acid for amyloid. Methyl green for hyaline.

Bronchi.—The increase in connective tissue around the bronchi was more considerable than in any other portion of lung substance. The lumens of the moderate-sized bronchi were very much misshapen, some of them appearing flat and slit-like; others triangular of the tubes show columnar epithelium, but the majority show a scant covering of bizarre epithelium. Many of them are entirely devoid of epithelial covering. The epithelium is set on a solid connective tissue base, consisting of dense fibers, which fibers are generally circularly disposed. In places this layer projects into the lumen after the fashion of an intracanalicular fibroma. In this layer, which seems to represent a compounding of all of the layers originally existing, except the epithelial

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lining, there is a great abundance of elastic fibers, as shown by Weigert's and other stains. Some areas in this layer show hyaline and glassy, but staining for amyloid and for hyaline with methyl violet; methyl green; Unna's and other stains gave negative results. The cartilage plates are in some instances bent at sharp angles.

The Blood Vessels.—There is very great thickening in the connective tissues composing the walls of the moderate-sized blood vessels found in the vicinity of the affected bronchial tubes. The larger blood vessels do not seem to have participated in this process. The appearance of the blood vessels is that of arteritis obliterans.

Alveolar Walls.—The alveolar walls show some thickening with interstitial tissue in all areas, except those that were emphysematous. This overgrowth of interstitial tissue is very much more marked in the peribronchial alveoli. Elastic tissue stains show a large amount of this tissue.

Gummata.—These show central necrotic tissue. Around this is a heavy fibrous wall, oftentimes of a hyaline appearance, but failing to take specific stains for hyaline. There are no giant cells. The old heavy comparatively cellular connective tissue is joined to the surrounding connective tissues.

Testicles.—These show heavy connective tissue continuous from the outside tunics and radiating so as to segregate occasional small parenchyma masses. There is thickening of the vessel walls.

Anatomically and histologically three varieties of syphilis are recognized:

The interstitial pneumonia type; the gummatous type; and the white pneumonia form.

It is true that there is interstitial pneumonia in the gummatous and in the white pneumonia forms. It is also true that occasionally gummata are found in the

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white pneumonia form, but in spite of this merging of types there are groups of cases considerable enough in numbers and clear-cut enough in type to justify each of the groupings. Observers from time to time have offered classifications showing subdivisions of the above, yet none of these have been established.

The white pneumonia is the type of syphilis found in the syphilitic child, born dead, or dying within a short time after birth. It is solid and pale in color. Its characteristics are:

1. A diffuse overgrowth of connective tissue.

2. The air spaces are (*a*) encroached upon by the growth of connective tissue; (*b*) undistended or only partially distended by reason of the fact that the child has never inspired, or, has only incompletely inspired; (*c*) filled, by alveolar epithelial cells in a state of fatty degeneration.

The pallor results from the causes already enumerated plus the anemia of vascular sclerosis.

Rarely gummata have been demonstrated in this form of disease.

The interstitial form is occasionally found alone, but more frequently it is a complicator of one of the other forms of lung syphilis. The term "found" is used advisedly, because it is not improbable that in many cases of tertiary syphilis specific diffuse interstitial pneumonia is overlooked. Certain it is that the picture of this form of disease is less easily recognized than that of the other varieties. Pankritrius, who wrote on this division of the subject, thought the lesion very frequent. Its histology is that of a productive inflammatory process in the peribronchial, periarterial, interlobular and alveolar interstitial tissue. I am not aware of any study of these changes (along the lines of Wieder and Herzog) with a view of determining in which of the elements of the vascular apparatus, to-wit: the arteries, veins, capillaries or lymphatics, the pro-

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liferative changes are most marked, or are primary. Independently of the cases in which gummata are recognized as such, Neuman cites statements to the effect that focal necrosis is demonstrable at times in specific diffuse interstitial pneumonia. It is exceptional to find the gumma type except as a tertiary lesion of syphilis in the adult. The lesion is so striking in appearance, that naturally it was the first variety described, as it is perhaps least frequently overlooked. Its resemblance to tuberculosis confuses not infrequently. This resemblance takes much of the value from the writings prior to 1880. It had something to do with the fact that Councilman, studying the cases of Carlier and Hiller, rejected over 60 per cent. of their 75 cases. I have recently looked up the writings of De Paul in 1853 and Lebert in 1857, and I find that they describe a suppurative process. Says Lebert: "We refer to a condition found in the syphilitic lungs of newly-born babies. These lungs one ordinarily encounters in a state of suppuration. This is why De Paul, who was the first to describe it in detail, mistook it for a multiple suppuration of the lungs. I have found in the lungs of a syphilitic child, newly-born, a gummatous tumor beyond question, in places softened and suppurating, showing all stages up to a true abscess." Says Neuman: "Many syphilitic affections of the lung parenchyma are overlooked because syphilis produces pathologic changes in the lung which are anatomically identical with those produced by other etiologic factors, and because these other factors are so much more frequent." On the other hand, it is possible that cases of syphilis have been hastily judged as tubercular. Porter (*N. Y. Medical Journal,* 1885) advocates this belief, citing figures drawn from his own experience—figures that certainly are in excess of our observations.

Still another group of cases must be borne in mind. Those in which the gummatous form of syphilis and the

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cavity-forming varieties of tuberculosis are associated. Schnitzler, Sanger, Potain, Neuman and Schiffermark refer to this association. Hodenpyl, among others, reports a case. In spite of the above, the gummatous form is the earliest and most certainly recognized. The gummatous masses range in size up to about the size of those exhibited here. Virchow, Neuman, Schiffermark, and, in fact, nearly all the observers refer to the dry crumbly character of the necrotic tissue. This necrotic mass is surrounded by a distinct capsule. Schiffermark says that the mass is not encapsulated. This, however, is not the usual holding. Councilman calls attention to the hyaline appearance of this capsule. The capsule generally sends bands of connective tissue that blend into the interlobular and alveolar connective tissue. The contraction of this connective tissue, as well as the increase, is responsible for a zone of consolidation circumscribing the area of gumma. With this view Councilman is at variance, as we will presently see.

There has been much controversy as to the seat of election of the gummatous nodes. Pankritrius said that the disease grew from the hilum. Leube says the primary localization is in the mediastinal glands. Leube refers to some who give the root of the lung as the primary location; others as giving the subpleural tissues. Porter thought the disease was usually apical. Councilman's cases showed that disease best toward the base. Schiffermark said that the disease was usually first located in the right middle. Says Neuman: "There are certain points, such as the middle portion near the hilum, and in the lower lobe, in which it is more frequently found than in the apex. Extending from the hilum these nodules develop along the bronchi. The general consensus of opinion is that the middle lung area and toward the hilum is the area of election. This was the location in this instance.

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There is much literature on the histology of lung syphilis. I will consider some of this. The following is a summary of the histology of this case:

1. A central necrosis taking a bluish stain with hematoxylin; 2, a heavy banded connective tissue capsule showing some hyaline areas. but failing to stain as does amyloid or hyaline infiltration; 3, an interstitial pneumonia with obliteration of air vesicles by (*a*) overgrowth of alveolar walls, (b) contraction; 4, areas of exudative and desquamative pneumonia; 5, focal round cell growth, the round cells being of the lymphoid type; 6, early necrosis limited to these areas, and not anywhere apparent in the areas of matured connective tissue growth; 7, connective tissue increase most markedly peribronchial; 8, evidences of general arteritis, phlebitis and lymphangitis; 9, bronchial lymphatic gummata.

Gummata.—Councilman says: "The essential process in the production of gummata in the lungs is a pneumonia with fibrinous exudation, accompanied by fibrous thickening of the old alveolar wall, the whole undergoing caseation. In the gumma the primary process is atrophy of the alveolar walls, due most probably to a hyaline degeneration. There is no leucocytic exudation."

Porter, in making a histological difference between tuberculosis and syphilis, says that in tuberculosis there is a peripheral zone of a vascular round cell tissue; in syphilis this zone is composed of vascular connective tissue. Schiffermark says: "In syphilis alone is the production of fibrous tissue a primary process." He quotes Virchow, as follows: "Above all is it necessary to have a connective tissue matrix." He quotes Birch-Hirschfeld as saying that microscopical diagnosis must rest on obliterative changes in the blood vessel wall. Neuman says that there is a growth of interstitial tissue, peribronchial, perivascular and alveolar. The alveoli are of normal size or dilated or compressed or filled with

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cheesy fibrin masses, with large granular epithelial cells, whose nuclei are still recognizable. In addition one sees scattered red blood cells and leucocytes.

Virrling, in speaking of a diffuse interstitial form with nodules scarcely distinct enough to be called gummata, says this is to be regarded as a variety of desquamative pneumonia separated from ordinary desquamative pneumonia by its location.

Blood Vessels.—The changes in the vessels have always attracted much attention. I have already cited Birch-Hirschfeld as insisting on these changes. Paolioneff says that the alveolar tissue is infiltrated with small cells and appears thickened. The small cells are mostly around the vessels. Neuman says wherever the process may be located, the vessels are diseased and the alveolar capillaries disappear before the new process appears. With the advent of the lumen obliteration the alveolar contents decompose, the alveolar framework and the alveolar septa become necrotic and there follow fatty changes and caseation.

Lancereaux says: "The gummata begin as a periarteritis and extend centrally by successive layers until the intima is reached." Endarteritis obliterans and death from starvation occur. Paul Lieneff says that the elements of new growth are arranged concentrically in the neighborhood of blood vessels whose adventitia is much thickened. The lumen is much decreased as the result of pressure and cell proliferation. I have already referred to Councilman's belief in the hyaline degeneration of the vessel walls. Rieder and Herzog claim that the changes are principally in the veins and in the lymphatics rather than in the arteries, and that the coats rank as follows in pathologic importance: Adventitia, intima, media.

Abramow, in describing the vascular changes in the coronary arteries, says that all of the coats of the vessels are involved. The change in the intima is an endo-

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thelial cell production, in the adventitia an overgrowth of cells, or rather an infiltration of cells. The changes in the media are those of granular degeneration. The changes in the intima are the earliest and most prominent. He saw a hyaline degeneration in the inner side of the intima as well as some mucoid change in its substance. Heubner and Wendeler observed the formation of a new fenestrated membrane. Abramow did not observe changes in the elastic tissue fibers.

Attention is called to the vascular changes in the specimens exhibited. I could not demonstrate the hyaline of Councilman. The vascular changes seemed to be limited to no coat. The vascular walls were welded in the general connective tissue masses.

The Bronchial Tubes.—Nearly all of the writers refer to the changes in the bronchial tubes. In Neuman's picture of the gross appearances much prominence is given to the bronchial tubes, which are described as, "injected, thickened, in places ulcerated, in places contracted, compressed, in places dilated into bizarre shapes." In none do I read of so great prominence of bronchial walls phenomena as are observable in the present case. Here the development of connective tissue is extreme, and in many of the tubes must have been completely obliterated eventually. The subepithelial connective tissue here seen does not form a proper base for the maintenance of epithelial vitality, hence the epithelial changes seen in these fields.

Many observers call attention to the fact that rupture into a bronchial tube rarely occurs. In the event of this happening, the atheromatous mass may be emptied into the tube, leaving a cavity which may cicatrize, may collapse and obliterate, or may become infected. None of these phenomena are observed here. Some attention has been directed to the lymphatic glands. Neuman says that certain authorities have termed the disease an adenopathy. Leube believes in an early location in the medi-

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astinal glands. In this case a large basal bronchial gland shows a well-marked encapsulated gummatous mass.

History.—The first form of syphilis that was recognized was the gummatous form. This form was probably described by Morgagni. There is some literature concerning it during the eighteenth century. Astruc, in 1738, gave a wonderfully clear clinical picture of lung syphilis. In 1809 Portal wrote. Laennec wrote in 1826. De Paul wrote in 1853. There is some doubt as to the accuracy of his writings. In 1857 Lebert treated the subject, devoting to it two pictures in his atlas volume of Traite d'Anatomie Pathologique. In 1858 Virchow wrote of the white pneumonia form. However, Hecker, in 1857, clearly connected this with the syphilitic processes. In 1863 Wagner wrote, adding much light to the subject. Lancereaux wrote in 1873; Paolioneff in 1879.

In 1881 Pankritrius made the diffuse interstitial changes and their relations to syphilis clearer than they had hitherto been. In 1882 Carlier collected a large number (67) of cases. In 1884 Hiller collected 75 cases, using Carlier's collection. In 1885 Porter reported that of a series of general postmortems extending over about eight months 26 per cent. showed evidence of lung syphilis. In 1891 Councilman wrote a valuable article on the subject in the *Johns Hopkins Bulletin.* Schiffermark wrote in 1896.

The most valuable articles that I have found in the productions of recent years are Neuman's contributions to Nothnagel's System, and Fowler's article in Allbutt's System. During the last ten years the *Index Medicus* records thirty-seven articles, mostly reports of individual cases. Of these thirty-seven articles in ten years, eight are found to be in American medical journals and by American authors.

In connection with the literature of to-day it may not be out of place to call attention to the infrequency of lung syphilis. Osler says that he has seen six cases.

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Councilman reported two cases. He scaled the cases of Carlier and Hiller to twenty-nine specimens, rejecting the remainder as non-syphilitic. Fowler says that in the museums of England he found twelve, of which ten were probably genuine. Leube devotes but little attention to the subject. Ziegler's attitude I should describe as tending to discredit the disease. Orth, in his smaller work, refers only to white pneumonia. Holt has but little to say. He say that in syphilitic children any inflammatory process tends to become necrotic.

March 12, 1900.

MULTIPLE OSSIFIED ECCHONDROSIS AND EXOSTOSIS OF THE TRACHEA AND LARGER BRONCHI.

I. B. DIAMOND.

The presence of bony and cartilaginous growths in the mucous membrane of the trachea has always been of interest, not only on account of their rarity, but also from the question whether they should be regarded as processes of a chronic inflammatory nature or be classed under the true tumors. Of the fourteen recorded cases the writers are almost equally divided in their opinion; only a few observers have found any connection between the new growths and the tracheal cartilages. Wilks,[1] Steudener,[2] Chiari,[3] Denig,[4] and Ganghofner[5] describe the nodules and plates as free within the mucous membrane, between and above the cartilaginous rings, and reaching as far as the subepithelial layer. Eppinger,[6] Heyman.[7] and Hammer,[8] on the other hand, found distinct connecting links between these growths and the

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tracheal rings and regard them as ossified ecchondroses, a view similar to that held by Virchow.[9]

The same differences of opinion exist with regard to their formation. Steudener, for instance, who found no cartilage in and among the bony masses, is of the opinion that the bone developed from the elastic fibers of the mucosa; Denig regards the process as a direct transformation of the connective tissue, the cells later changing into bone corpuscles; while Ganghofner comes to the conclusion that the inflamed connective tissue first changes into cartilage and then into bone. Hammer, who studied altogether seven cases, including the published cases of Chiari and Eppinger, comes to the conclusion that all these bony tumors are developed directly from the tracheal cartilage and are finally transformed into bone. The outgrowths develop in a fungus-like manner, arising from the perichondrium by a stalk or stem, which sooner or later undergoes branching; the stems being usually thin but broad, and for that reason many sections have to be cut to find them. Hammer believes that this explains the fact that many have failed to find the connecting links between the new growths and the tracheal rings. Heyman comes to a somewhat different conclusion. In his case there was only one area which showed any connection of the bony masses with the perichondrium in which were evidences of proliferation; and for that reason he is inclined to the views of Virchow, namely, that the peripheral sections of the cartilage and perichondrium at certain portions undergo proliferation, and grow beyond the limit of the rings into the mucosa. As a growth advances the connection between it and the matrix grows gradually thinner, until it is finally severed, changing later into bone.

Whether the tracheal cartilage also takes an active part in the process is doubted by Recklinghausen.[10] He believes in a metaplasia of certain connective tissue bands which radiate from the perichondrium into the mucosa

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and become transformed into cartilage and osseous tissue, rather than an active proliferation of the tracheal cartilage; since the cartilage of the new growth is reticular and elastic, resembling, as pointed out by Virchow, the cartilage of Santorini (cornicula laryngis).

It is remarkable to what an extent the upper respiratory tract may become involved by these growths. They have been described extending from the larynx to the finer bronchi. The nodules may be single, but are usually multiple, or they may be united into several masses, varying in size from a millimeter or two to several centimeters; and, when consisting of bone, there may be solid blocks of canalized bone with Haversian canals and marrow spaces filled with fat and blood vessels.

The case now reported involved the entire trachea and larger bronchi of a man 48 years old, who died at Cook County Hospital of pneumococcus spinal meningitis and bronchopneumonia.

Description of Gross Specimen (Fig. 1).—The cartilages of the larynx are calcified; the mucous membrane is smooth and grayish in color, otherwise normal. The trachea is hard, rigid, and inflexible, as though it were in a cast. This fixed rigidity is due to irregular grayish masses which cover the entire interior surface of the trachea. These masses are situated beneath the mucous membrane, are rough and ridged and of bony hardness. The masses begin at the under surface of the second cartilaginous ring, filling out the membranous interspace; but a little lower down they spread above the rings, covering them. On the right lateral half they are thicker and more corrugated. As they approach the sixth cartilaginous ring they encroach upon the median line, fusing together into one reticulated mass. Deeper down the trachea this latticed mass becomes more prominent until it reaches the bifurcation, when it separates to either side, becoming finally lost in the larger bronchi. As the mass becomes separated, it again assumes its nodular

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character, breaking up into many smaller masses. Slightly above the bifurcation, and to the left, is a pear-shaped body, irregular on its surface, and situated upon and between two rings which meet. It is about one centimeter in diameter and fuses at one point with the masses on its left. The masses in the bronchi have the same appearances as those described in the trachea, with the exception that they are less developed and not so reticulated.

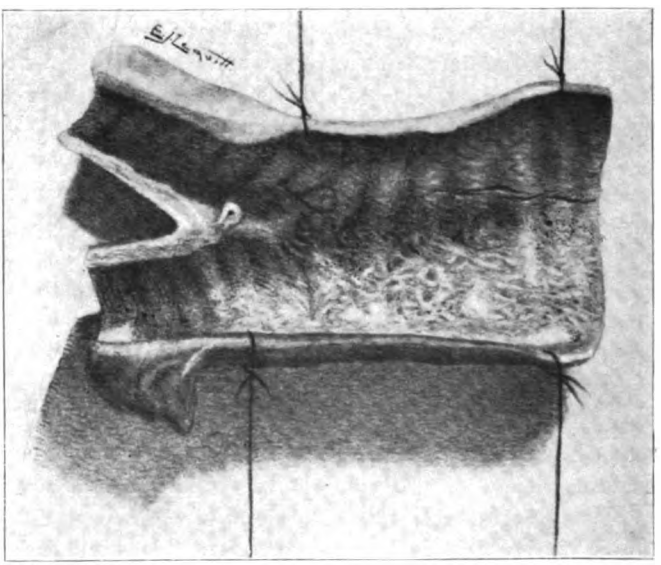

Fig. 1.—Showing trachea and bronchi. Opened from behind. The inner surface is corrugated; this is especially marked on the right lateral half, where it resembles lattice work. To the left and above the bifurcation is a pear-shaped body, situated between and above two rings.

Microscopical Examination.—For a microscopical study a piece of the trachea was decalcified, hardened in alcohol and formalin, embedded in paraffin, cut, fixed on slides, and stained with hematoxylin and eosin, Van Gieson, Weigert's elastic fiber stain, etc.

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Transverse sections from within outward show the following changes (Fig. 2): The columnar epithelium is flattened and has lost more or less its epithelial character. The epithelial layer projects here and there so that the inner surface of the sections has a wavy appearance. This is due to irregular, pinkish, homogeneous bodies, which are situated beneath the epithelial layer. Some of these bodies are solid, others contain spaces, which are filled with blood vessels, small, deeply staining cells, and fat-like spaces. These various sized plates extend throughout the subepithelial layer, some are connected by branches with each other, others are free, and some again are united by bands of connective tissue, which has lost its fibrillary structure and is homogeneous and dense. Some of these branching masses extend down as columns into the submucosa and are united to the internal perichondrium. In some sections the columns form complete irregular rings, united or fused below with the perichondrium and above with the mass situated beneath the epithelial layer. By this union smaller or larger spaces result which are filled with fatty marrow. Partially surrounding some of the plates are several layers of cells enclosed in capsules and embedded in a homogeneous ground substance; and around these layers again are collections of small, deeply staining cells, containing numerous distended capillaries. The submucosa is largely converted into an areolar tissue, infiltrated here and there by collections of round cells and capillaries. Nests of cartilage cells are also present, which vary in size from one-half to several millimeters; these are usually embedded in the round-celled accumulations. It is reticulated in structure, and the cells are enclosed by capsules. The mucous glands are swollen, some are granular, while others again have undergone atrophy or have disappeared. They are all infiltrated by the same small, round, deeply staining cells. Scattered throughout the mucous membrane are patches of connective tis-

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sue, dense and of a homogeneous appearance, resembling scar tissue. The cartilaginous rings are somewhat thickened; the cells are increased in number; many stain deeply with hematoxylin, others again are swollen, irregular in shape, or undergoing proliferation. The ground substance is dense and infiltrated with calcium salts (calcified). The perichondrium is greatly thickened, opaque, and homogeneous in appearance, and in many sections stains in the same way (hematoxylin and eosin) as the plates and masses beneath the subepithelial layer. Its inner surface is irregular and rough in outline, due to small projections, while near the median line the perichondrium projects like a stalk or stem into the submucosa. This stalk is only seen to advantage in one or two sections, and not being very thick, is soon lost in other sections. A little above its base the stalk branches. The smaller of the two is united to a shoot or twig, which springs from one of the subepithelial plates by an intervening band of connective tissue, while the larger branch which extends to the right soon divides into two smaller branches. This right branch also is united by a band of connective tissue to the plate above as well as to the branch to its left. By looking through many sections it is found that the branching subepithelial plates are offshoots of the stems arising from the perichondrium, which divide and subdivide, forming complete, irregular, bony rings. Besides the large stalk there are smaller ones, which also arise from the perichondrium. These are more delicate; they also divide and subdivide, and as observed in some of the sections are united with each other, forming complete or incomplete rings. These stalks, as well as the branching subepithelial plates, are made up of one and the same structure, namely, of concentric or irregular lamellæ, among which are scattered elongated nuclei, each of which is enclosed by an irregular capsule or space.

From these appearances it is evident that we have to

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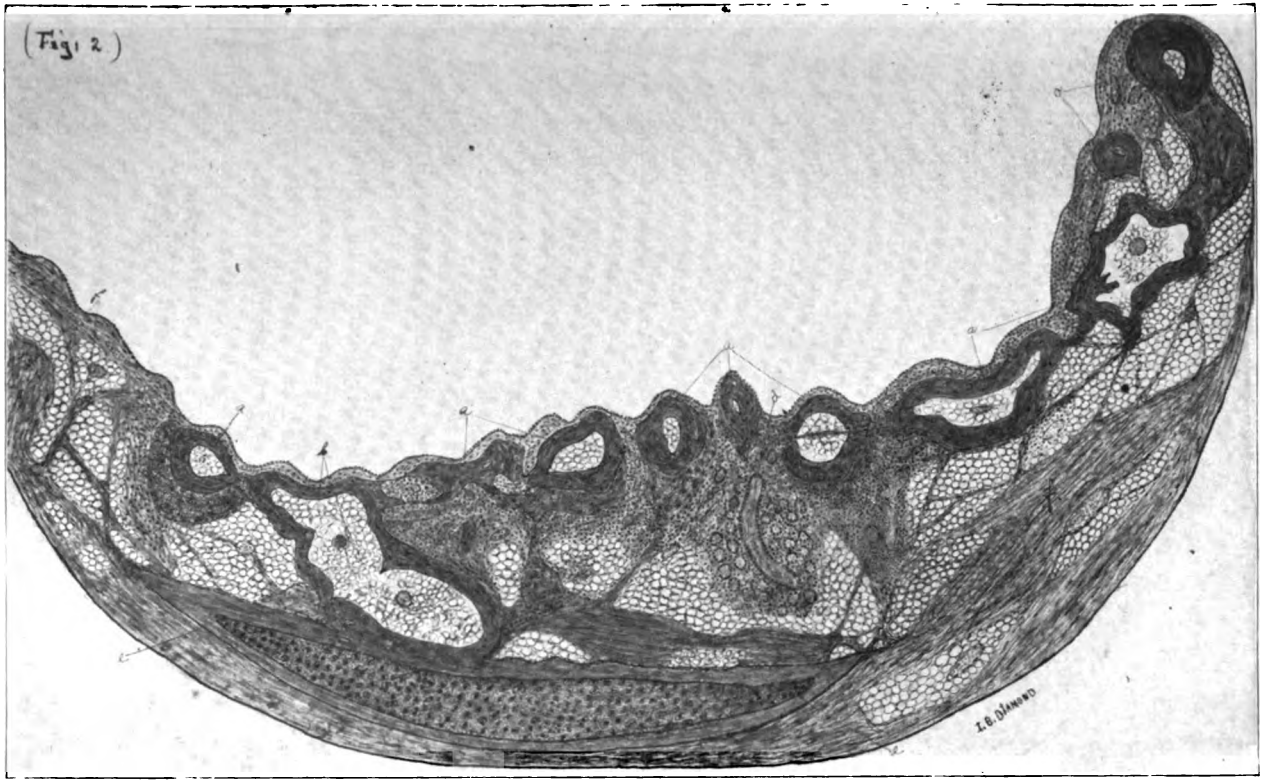

Transverse section of trachea, low power (hematoxylin and eosin): (*a*) Branching subepithelial bony plates; some are partially surrounded by cartilage; (*b*) ring-like exostoses filled with yellow marrow; (*c*) bony masses embedded in round-celled accumulations; (*d*) mucous glands; (*e*) tracheal ring showing thickened perichondrium; (*f*) connective-tissue patches and fat spaces.

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deal with the formation of true bone, which not only is made up of concentric lamellæ, lacunæ, and canaliculi (Haversian system), but also contains spaces filled with yellow marrow. These arise from the perichondrium (by stalks or stems), and are therefore to be regarded as true exostoses. Not all of the subepithelial plates, however, are connected to the perichondrium by true bone, but are separated from it by solid blocks of cartilages—in other words, by true ecchondroses, as they arise from the perichondrium by bands of connective tissue which interlace and surround the cartilage blocks, giving them a reticulated appearance. The upper portions of the cartilage upon which the subepithelial plates rest and into which they gradually fuse do not show this reticulated structure. The ground substance is more homogeneous, denser, the cartilage cells are smaller, more elongated, and evidently changing into bone corpuscles. This transformation of the cartilage into bone is beautifully shown by Weigert's elastic fiber stain. The bony nodules stand out as pinkish, creamy bodies, in striking contrast to the purplish-red cartilage masses. As the cartilage gradually changes into bone, the red color of the ground substance becomes lighter, and here and there are seen spots of beginning ossification. The elastic elements which are brought out so beautifully by this stain are prominently developed. They run in every direction as fine threads or twigs, interlacing with each other, penetrating as well as surrounding the cartilage and bony masses. Fine twigs are also seen among the collections of round cells and surrounding the walls of minute capillaries. They run as thicker threads beneath the subepithelial layer, in the perichondrium (outer as well as inner surface), and are here and there broken up into fragments. Surrounding the bony and cartilaginous masses they form a thick network, standing out almost as bluish-black cords.

As mentioned before, many of the bony nodules are

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isolated and free, surrounded either by cartilage or are embedded in a mass of connective tissue cells rich in blood vessels. Here it seems as if the connective tissue cells change directly into bone corpuscles, without the intermediate stage of cartilage, as the connective tissue immediately surrounding the bone appears homogeneous, while the cells are more elongated, some being encapsulated. This growth by apposition is also described by Denig and Arnsperger;[11] in our case, however, this mode is the exception and not the rule.

The recent publications of Manasse[12] and Glockner[13] on amyloid tumors of the trachea in which bone and cartilage were also present induced me to stain sections for amyloid. In the few sections thus treated it was either absent or the material did not react to the stains. Schmidt[14] previously emphasized that a certain relation exists between the formation of bone and cartilage on the one hand and amyloid on the other. Amyloid is now thought to be closely allied chemically to elastic fibers and cartilage (chondratin-sulphuric acid with a proteid), hence Glockner enlarges Schmidt's statement to the effect that local amyloid is found in organs which are rich in elastic elements and cartilage. For similar reasons he explains that the presence of bone and cartilage in amyloid tumors is the result of a metaplasia of connective tissue, rich in elastic elements. That they play some part in this process is evident, for they are plentifully developed in the cartilaginous outgrowths. Furthermore, it verifies Recklinghausen's belief, that the normal tracheal cartilage does not take an active part in the production of the outgrowths, but that the latter wholly arise from the perichondrium.

There is one point yet to be noted with regard to these outgrowths: On the one hand, we have, as previously described, seemingly true exostoses arising from the perichondrium, while on the other only ecchondroses. Are both to be regarded as distinct processes, or do they rep-

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resent different stages of the same process? What seems at first so confusing are the stalks which Hammer regards as typical in these outgrowths, and of which I find so few in the exostoses and none in the ecchondroses. From the microscopical appearances of the sections I have come to the conclusion that the stalks are but parts of bony rings. The rings are formed by the branching subepithelial plates above and by the perichondrium below. Now in certain sections the rings are found incomplete, the connection with the perichondrium is wanting; but when we compare these sections with those containing the stalks, we find that the stalks are portions of incomplete rings, which connect them to the perichondrium and which have become severed in sectioning. These bony rings I believe are derived from ossified ecchondroses. Their development is to be explained in the following manner: The cartilaginous outgrowths, as they approach the subepithelial layer, being connected with each other, either through connective tissue bands or cartilage, become metamorphosed into bone (Fig. 3), starting from above downward. This new bone is at first solid and composed of concentric lamellæ, which constantly increase in extent. As this goes on the central area of the bone becomes canalized, probably by absorption, as in a few of the spaces I have seen multinuclear cells, which probably play the rôle of osteoclasts. The process gradually extends until the whole mass of new bone is converted into a large ring, reaching to the perichondrium. All the smaller subepithelial plates are nearly surrounded or capped by a shell of cartilage; the larger the spaces, the less cartilage surrounding the bone, indicating a more advanced process. The larger rings are devoid of cartilage and made up of only one or two lamellæ of bone. By comparing the original ecchondroses with the ring-like exostoses we note how nearly alike they are in diameter, showing that we

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are dealing with various stages of the same process and not with two distinct conditions.

This mode of transformation of the cartilaginous outgrowths into bony rings it seems to me would explain in a manner the different conclusions reached by various observers. For as the process continues, outgrowths may become entirely separated from the perichondrium, not by connective tissue growth from outside, but by absorption from within, which constantly enlarges the space until the ring is completely severed from the perichondrium. When sections are examined at this stage the connection with the perichondrium is lost, and the subepithelial plates seem to have developed free in the

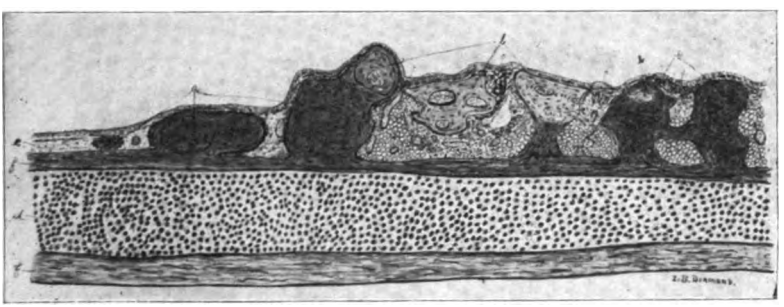

Fig. 3.—Transverse section of trachea, low power (Weigert's elastic fiber stain): (*a*) cartilaginous outgrowths; (*b*) subepithelial bony plates, which are situated above and within the cartilaginous outgrowths; (*c*) elastic fibers, surrounding the bony and the cartilaginous masses; (*d*) tracheal ring; (*e*) submucosa; (*f*) perichondrium.

mucous membrane. For this reason many observers have regarded the growths as true tumors. Maischikoff,[15] for instance, advances the theory that they are the result of an anomaly in the development of the tracheal rings. He says the tissue which serves as ground substance for the future tracheal rings has spread beyond the boundary line into the mucosa. In this tissue there may be formed cartilage. Later the misplaced cartilaginous areas are

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metamorphosed for some unknown cause into bone. This statement of course can not hold, in the face of our findings. Traumatism and various chronic inflammations in the mucous membrane would seem to be the essential factors in the production of these outgrowths. In the case of Heyman there were marked chronic inflammatory changes in the mucous membrane with a suppurative perichondritis which had perforated into the esophagus. Hammer, who investigated all the reported cases, divides them into two groups. In the first, as a result of syphilis and rhinoscleroma a chronic inflammation of the mucous membrane of the trachea existed leading to scar formation, reaching as far as the perichondrium, and causing the perichondrium to proliferate. Under this head belong the cases of Ganghofner, Chiari, Heyman, and two of his own cases. In these cases scars were present in the mucous membrane which led to stenosis. Syphilitic lesions were also found in other parts of the body. The second group comprises all those cases in which no chronic inflammatory processes could be demonstrated in the mucous membrane of the trachea. These are the cases in which the growths have been regarded as true tumors. Almost all occurred in old persons, in whom senile calcification of the tracheal rings existed; besides, there were chronic catarrhal inflammations of the respiratory tract, as bronchitis and tuberculosis. Chronic interstitial inflammation is regarded by Arnsperger as the exciting cause of bone formations in the lungs. The fact that trauma may play some part has, I believe, been overlooked. An analogous case is reported by Cohen.[16] A man kicked by a horse in the thigh soon developed a swelling of bony hardness in the muscles of the thigh, which later, on removal. was found to have sprung from the periosteum of the femur. It is therefore possible that injuries, blows, etc., to the upper portions of the trachea or larynx may excite a perichondritis followed by subsequent out-

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growths, for they usually start at the upper portion and frequently begin in the larynx. Unfortunately, in our case no history was obtainable. There were present, however, some senile changes. The aorta showed an arteriosclerosis, while one of the peribronchial lymph glands was calcified. The spinal dura and pia were also calcified, and in the left lung was an encapsulated caseous focus. Of course, we can only conjecture as to what relation these conditions bear to the growths. There was present in the mucous membrane of the trachea considerable round-celled infiltration—granulation tissue—and patches of scar tissue, while the tracheal rings were calcified; and with the outgrowths we have a typical picture of a chronic inflammation. Whether the outgrowths were secondary or not I am unable to say. It is remarkable that nearly all of the cases have died from some pulmonary affection, namely, tuberculosis, abscess, or gangrene of the lungs. It would seem that as a result of this condition the respiratory tract is weakened against the invasion of microbes, especially since the epithelial cells are changed, even destroyed.

As to the clinical significance of these growths very little is to be said. They are rarely if ever recognized during life, except when situated at the upper portion of the trachea, and grow to such size as to interfere with respiration. A case of this kind is reported by Jackson[17] in a man who complained during life of dyspnea. At autopsy he found a cartilaginous tumor about two inches below the larynx, which occupied about one-half of the passage. When situated in the larynx they are readily recognized and even successfully removed. These growths, however, are almost all cartilaginous in nature. Cases of this kind have been reported by Stoerck,[18] a number by Bruns and Putelli,[19] and in this country by Asch,[20] Ashhurst,[21] Musser,[22] Solis Cohen,[23] and Ingals.[24]

June 11, 1900.

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E. R. LE COUNT demonstrated specimens showing retrograde carcinoma in the lymphatics of the lung.

Feb. 11, 1901.

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CIRCULATORY SYSTEM.

RARE CARDIAC ANOMALIES.

CONGENITAL AORTICO-PULMONARY COMMUNICATION; COMMUNICATION BETWEEN THE AORTA AND THE LEFT VENTRICLE UNDER A SEMILUNAR VALVE.

BY LUDVIG HEKTOEN.

In the following will be described two decidedly uncommon defects—one of the septum between the pulmonary artery and the aorta, and the other of the base of the right anterior aortic valve, the latter being, as far as I can tell, absolutely unique. The patients, two newborn infants, died in the Presbyterian Hospital while under the care of Professor Cotton, and the postmortems were made in my laboratory. Both cases have been previously recorded by Professor Cotton,[1] but with especial reference to certain clinical manifestations, particularly anuria, hence the reason for this additional report.

1. *Large defect in the septum between the pulmonary artery and the aorta, the heart normally developed; general infection with B. mucosus capsulatus. Postmortem* (675).—Well-developed, fairly well-nourished male infant, 51 cm. long. weighing 2657 grams. There are no external malformations. The surface of the body, both anteriorly and posteriorly, is bluish-red in color. The umbilical cord is dry and separating at the navel. The abdomen is somewhat distended.

The abdominal cavity is empty, the lining smooth. The diaphragm reaches to the fifth right and sixth left ribs.

The pleural cavities are empty and smooth as to lin-

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ing, the visceral pleura being the seat of many hemorrhagic extravasations.

The pericardium is also smooth, the cavity contains a small amount of clear fluid.

The mouth, pharynx, larynx, trachea, and espohagus are normal. The thyroid is of usual size; the thymus rather small.

The lungs are fully distended and show many small, deeply-congested spots throughout the parenchyma; no bronchitis.

The heart presents a much larger right than left ventricle; the latter is situated more behind the right than usual. The walls of the two ventricles are of about the same thickness, but the cavity of the right ventricle is much the larger. The tricuspid and mitral valves are quite normal; the pulmonary and aortic valves are also well formed and normal. There is an oval defect, about 1.5 cm. in its greatest diameter, between the pulmonary artery and the aorta, so that a little above their beginning the aorta and the pulmonary artery have a common trunk from which emerge in the usual places, relatively, the right and left pulmonary arteries and the branches of the arch of the aorta (Fig. 1). The greatest diameter of this common trunk is 3 cm. Between the semilunar valves arises a septum with a somewhat rounded, concave upper margin; from the base of the pulmonary semilunars the septum rises to a height of 3 mm., while from the base of the aortic semilunars the septum is 1 cm. high. The ductus arteriosus is fully patent and quite large, and the part of the aorta distal to the duct is wider than the transverse part proximal to the duct. The foramen ovale is widely open. The veins—pulmonary and caval—are quite normal. The ventricular septum is normal.

The stomach and intestines are normal.

The pancreas is normal.

The liver and spleen are congested, the liver being

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soft and mottled, yellow and red. The spleen weighs 10 grams, the liver 110 grams. The adrenals are normal, weighing 11 grams.

The urogenital organs are normally formed and situated. The bladder contains a small amount of turbid urine, the mucous membrane immediately about the

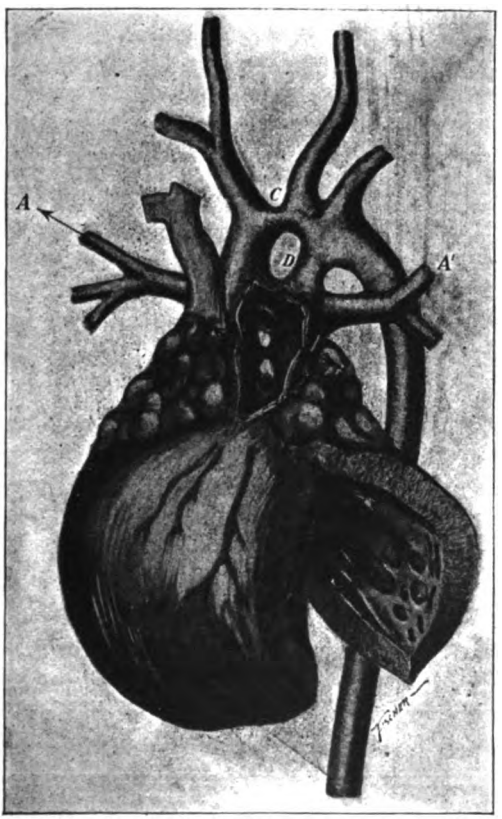

Fig. 1.—Aortico-pulmonary communication. *A*, right pulmonary artery. *A*[1], left pulmonary artery. *B*, opening of aorta from left ventricle into common trunk. *C*, partial obliterated aortic arch. *D*, large patent ductus arteriosus. *E*, hypertrophied right ventricle.

ureteral orifices is swollen and red. There is no dilatation of the ureters and pelvis. There is marked uric

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acid infarction in both kidneys with some congestion of the pyramids. The kidneys weighed 26 grams.

The brain and its membranes are normal; weight, 1381 grams. The lines of ossification are even and regular; Bichat's center measures 4 mm.

Bacteriological Examination.—Smears and cultures from the heart's blood, the lungs, the liver, the spleen, and the kidneys all show a bacillus with the morphological, cultural, and pathogenic characteristics of bacillus mucosus capsulatus.

Histological Examination.—The heart shows normal structural conditions.

The lungs are the seat of an extensive hemorrhagic infarction, the alveoli and bronchioles in places being filled to distention; otherwise no changes.

The liver is the seat of a marked passive congestion with fatty infiltration of the liver cells and some recent increase in the periportal connective tissue, which is rather cellular.

The cortex of the kidney shows cloudy swelling of the epithelium of the convoluted tubules. In the medulla the uriniferous tubules are crowded full with a granular material which stains light blue with hematoxylin; the epithelial lining is intact and the vessels uniformly distended with blood.

Sections stained with methylene-blue show occasional encapsulated short bacilli here and there in all the organs, especially among extravasated corpuscles and in the capillaries of the lungs.

Instances of direct communication between the aorta and the pulmonary artery, caused by congenital defect in the septum of the arterial trunk, are described by Elliotson,[2] Wilks,[3] Fräntzel,[4] Baginsky,[5] Cæsar,[6] Girard,[7] and Richards;[8] Rauchfuss[9] and Gerhardt[10] also each mention an instance. These seem to be all the instances recorded in literature. The defect is rare. Virchow, in discussing Baginsky's case, remarked that he

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had not seen an example before. As far as I have been able to learn, there is no previous instance recorded in American literature.

In all these instances (except Richards' case) there is a simple communication between the aorta and the pulmonary artery, the opening being situated a short distance above the semilunar valves, round or triangular in outline, and 10 to 12 mm. in diameter. Other malformations are not noted, and evidences of endocarditis or angeitis are wanting altogether. This form of communication is consequently of congenital nature, and it is to be distinguished from the more frequent, similarly located communications of acquired, accidental origin.[11] It is also to be held distinct from communication between the pulmonary artery and the arch of the aorta through a persistent ductus arteriosus, which, when uncommonly short, may lead to a close approximation of the two vessels. The location of this communication would be different, namely, at the arch of the aorta.

Closely related to direct congenital communication between the pulmonary artery and the aorta is congenital communication between the beginning of the aorta and the right ventricle. Such cases are described by Cayla,[12] Charteris,[13] and Livingston.[14] In Cayla's case (man, aged 34) a canal passed from the upper part of the ventricle into the aorta just above the valves, which was somewhat irregular. Quenu suggests that the defect was caused by failure of union between the septum of the bulb and the interventricular septum. Charteris describes an opening "immediately under" the right valvular aortic curtain communicating with the right ventricle. This occurred in a man, aged 53 years, and perhaps a question might be raised as to its congenital nature.

Livingston's case occurred in a child four months old. Just at the beginning of the aorta a communication led into the right ventricle. There were only two aortic

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TABLE OF CASES.

No.	Author.	Age.	Sex.	Clinical symptoms.	Description of the defect.	Ductus arteriosus.	Remarks.
1	Elliotson	Young	F.	. . . . .	Opening admitted end of finger.	Closed.	No other anomalies.
2	Wilks	8 mo.	. .	Strong systolic bruit at base; no cyanosis; ascites.	Opening admitted goose-quill.	Closed.	Pulmonary artery large, aorta small; no trace of inflammation; no other anomalies.
3	Fräntzel	25 yrs.	F.	Dyspnea and palpitation as long as she had memory. Increased cardiac dulness; dropsy; cyanosis; changing auscultatory phenomena; at first systolic and diastolic murmur; later diastolic murmur was replaced by double tone; dyastolic murmur same distribution as in aortic insufficiency.	1 cm. above margin of aortic valves a round opening 12 mm. in diameter.	Closed.	Dilatation and hypertrophy of heart; right pulmonary artery originated from aorta just below arch; coronaries normal; no endocarditis; thrombi in left ventricle; innominate, common carotid, vertebral and left subclavian given off by arch; anasarca. (Postmortem by Cohnheim.)
4	Baginsky	4 yrs.	F.?	Under observation since 8 days after birth; there was cough, dyspnea, hoarseness, cardiac irregularity, systolic and diastolic murmurs and repeated disturbances of compensation; scarlet fever and nephritis Death from whooping cough.	Opening between aorta and pulmonary artery 1 cm. in longest diameter; margins somewhat thickened; almost triangular in outline; base on level with upper border of left pulmonary semilunar valve and 5 cm. above free margin of aortic valves.	Closed.	Parenchymatous nephritis; hypertrophy of both ventricles, more of the right, the left being the one most dilated.
5	Gerhardt	5 mo.	F.	No details except rough sound over heart.	Rounded opening with sharp margins.	. .	No endocarditis; specimen in Museum of Guy's Hospital.
6	Rauchfuss	Nursling		No details	No details	Closed.	
7	Cæsar	9 yrs.	M.	Cyanosis since three months. Passed through measles, bronchitis, pneumonia; otitis 1-3 year; right hemiplegia since 5; died at 9 in convulsions; no murmurs.	Communication between aorta and pulmonary artery size of a sixpenny.	Not stated	Marked fenestration of aortic valves; ascending aorta as large as an adult; pulmonary and meningeal tuberculosis; large chronic abscess with calcareous mass in l. hemisphere.
8	Girard	37 yrs.	M.	Smallpox at 1; dyspnea and cardiac distress since then; otitis; severe fever at 20, with swelling of legs; also other illnesses. Four years before death: dyspnea and hematuria; systolic murmur with accentuation of 2d sound. Clinical diagnosis: mitral insufficiency, renal embolism, hematuria. Shortly before death: dyspnea, cyanosis, gallop rhythm, enlargement of heart.	11 mm. above free edge of aortic valve opening into pulmonary artery 10 mm in diameter; no change in intima of aorta and pulmonary arteries.	Not stated, probably closed.	Heart weighed 670 grams; hypertrophy especially marked of right side; thrombus in apex of right ventricle; endocardium normal; coronary orifices large; extensive congenital tuberculosis.
9	Richards	30 yrs.	M.	Brassfounder until 3 months before death. Two loud, systolic and diastolic murmurs; hypertrophy of heart; dyspnea; anasarca.	Behind larger of bicuspid aortic valves circular opening into pulmonary artery admitting little finger; margins membranous, smooth; passage somewhat funnel-shaped.	Not stated	Hypertrophy and dilatation of heart; no endocarditis; pulmonary artery dilated above opening from aorta; defective interventricular septum.
10	Cotton-Hektoen	3 days.	M.	"Blue baby." Anuria	Oval defect 1.5 cm. in its greatest diameter in septum above semi-lunar valves.	Patent, rather large.	Foramen ovale open; no other defects; right ventricle hypertrophied.

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valves. White[15] and Tate[16] also describe somewhat similar defects. Lediberder's[17] case was more complicated. Here there was pulmonary stenosis, closed foramen ovale, open ductus arteriosus, and communication between pulmonary artery and aorta. I have not looked up the details.

In White's case (boy. aged 15 years) the whole upper septum was deficient in thickness, and there was failure of complete closure at the right of the "undefended space." A small aneurysm had formed behind the right aortic valve and ruptured into the right ventricle.

Tate describes a trumpet-shaped membranous tube extending from a rounded opening at the lower part of the anterior aortic valve into the right ventricle. At the same time there was a saccular projection in the right ventricle at the "undefended space."

Congenital communication between the pulmonary artery and the aorta are to be traced back to developmental anomalies of the septum that divides the primary arterial bulb into two large vessels. A defect of this sort dates from some period of intra-uterine life before the seventh or eighth week, because at this time the pulmonary artery and the aorta are completely separated (Born,[18] His[19]). Based upon the presence of fenestrations of the aortic valves in the case of aortic and pulmonary opening described by Cæsar, H. Vierordt[20] suggests that the septal defect may be the result of an extension to the arterial wall of the process of hollowing out, whereby the primary endothelial cushions are converted into thin leaflets. At all events, the uncomplicated nature of the defect in most of the cases, including the one now reported, indicates that the defect is the result of abnormal developmental processes rather than of inflammatory changes (endangeitis). Similarly, communication between the aorta and the right ventricle may be ascribed to faulty development of the aortic septum; complete union between the interventricular sep-

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tum and the aortic septum may fail to take place during the time that the conus arteriosus takes up part of the auriculo-ventricular orifice (about the seventh week—Born).

The clinical features of direct congenital communication between the pulmonary artery and the aorta are considered by L. Brocq,[21] H. Vierordt,[22] and Leon Cazin.[23] The latter author made the clinical diagnosis of this lesion in a young woman, but in the absence of post-mortem examination its correctness will always be open to doubt. L. Brocq[24] shows that the location and the mechanical consequences of congenital aortico-pulmonary communications are the same as in accidental communications; but in the first the lesions are more pure, hence the true symptomatology should be sought in the congenital form; but the number of instances of the latter is as yet rather small for drawing a definite clinical picture. In most of the recorded cases the lesion was a surprised revealed by the autopsy.

The cases are equally distributed between the sexes. The age attained varies from a few hours to thirty-seven years.

In all the cases that died at an age of from four to thirty-seven years definite symptoms of heart disease were present; in three of them the heart lesion seems to have been the cause of death (Fräntzel, Baginsky, Richards); in two the cardiac disease was complicated by meningeal and urogenital tuberculosis (Cæsar, Girard). In the case now reported there was a general and marked infection with B. mucosus capsulatus.

By reference to the table of cases it is seen that the statements with respect to cardiac murmurs vary much. The most common murmur is a double one—systolic and diastolic—at the base; in Girard's case there was also persistence and accentuation of the second sound. In several cases the changing, uncertain character of the murmur is noted.

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Occasionally hypertrophy of the heart, especially at the right ventricle, quite commonly noted at the autopsies, was demonstrated by the physical examination. In all cases where the condition of the ventricle was noted there was found more or less hypertrophy, sometimes only of the right ventricle, but occasionally of both, the right being the larger; the reason for this being that the right ventricle contracts against the current sent out by the left side of the heart, which is the naturally stronger side.

Dyspnea, cyanosis, ascites, and anasarca were present in Fräntzel's case, and in Baginsky's, Girard's, Richards', and Wilks' cases some one of these evidences of grave disturbance of the compensation are noted, cyanosis being definitely mentioned by Cæsar and Girard, as well as Fräntzel; but the statements in regard to cyanosis are hardly definite enough to determine whether it was due to the defect itself or to the resulting cardiac insufficiency. In the infant that I examined cyanosis was fairly well marked. In this case there was also complete anuria.[25]

2. *Regurgitation through smooth depression under base of anterior aortic valve, which is attached to and carried across by a tendinous bridge; hypertrophy of the heart; dilated arterial duct; congestion. Postmortem* (838).—A well-developed, well-nourished female, newborn child; the body still warm; the umbilical cord is dry and there is a line of separation around its insertion at the navel; rigor is strong; the surface of the body is livid.

The serous cavities of the trunk are empty; their linings smooth. The diaphragm reaches to the fifth ribs.

The pharynx, larynx, and trachea are normal. The thymus and thyroid are normal. The lungs are distended and contain many areas of hemorrhage, subpleural and deep-seated. The lungs crepitate freely; no bronchitis; much congestion.

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There are subepicardial extravasations at the base of the heart. The heart is distended with blood. There is great enlargement of the heart, especially the left ventricle. From base to apex the heart is 4.5 cm. long and 5 cm. across the widest base. The heart weighs 42 grams. The endocardium of the right side is normal. The depth is 4 cm.; the wall is 3 mm. thick. The tricuspid orifice is 1 cm. in diameter. The foramen ovale is patent, and the ductus arteriosus is large and widely open, the aortic orifice of the duct measuring 6 mm. across; it is normally located. The pulmonary artery is normal. The

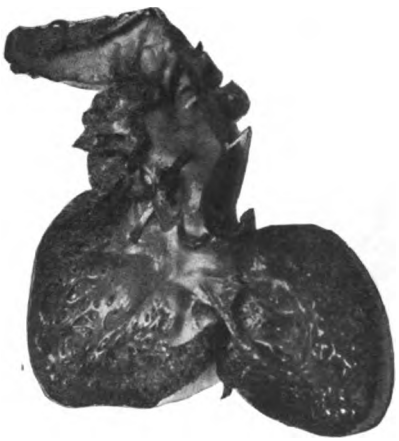

Fig. 2.—Bulging at aortico-septal junction and communication between aorta and left ventricle under anterior aortic leaflet.

mitral orifice is small—about 0.5 cm. in diameter; the auricular surface of the valve is smooth, but somewhat nodular, and there are also slight thickenings upon the chordæ tendineæ; no ulceration; no thrombosis. The aortic valves are large, higher than normal (about 6 mm.), of irregular thickness, but smooth, there being small, delicate, reddish nodules upon them, so that they appear somewhat deformed.[26] There are no distinct lunulæ or corpora arantii. There are three valves, but the anterior segment is attached to an irregular, dense,

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and firm, band-like bridge, 2 mm. thick, which extends across an oval depression in the upper part of the interventricular septum and the lower aspect of the aorta, which here presents a marked bulging anteriorly between the aorta and pulmonary artery (Figs. 2 and 3). It looks as if the lower end of the aorta and the interventricular septum had failed to develop fully. The junction of the septum and of the aorta occurs under the bridge, the line of exact junction being rather indefinite. The depression is 1.5 cm. vertically, 1 cm. across, and 8 mm. deep. The bulging is smooth, and there is no communication between it and the pulmonary artery or the left ventricle. The left half of the upper limit of the depression is marked by a rather sharp ridge in the aorta, but the right half is marked by a rounded bulging. Viewed from the right ventricle the "undefended space" appears as a triangular area near the center of the depression in the aorta. The interventricular septum is not perforated. The left ventricle is 1 cm. deep, and the wall is 5 mm. in average thickness. The beginning of the aorta, just above the sinuses of Valsalva, is wider than usual, but smooth; it is 2.5 cm. in circumference.

The right coronary arises in the deep sinus behind the anterior semilunar valve, near the right end of the bridge. Its distribution is normal; some of the branches at its beginning are rather large.

The left coronary arises in the sinus of the left posterior semilunar valve; the opening is a little higher than the right. The upper margin of the sinus is outlined by a rather sharp ridge.

The liver is large, congested, bluish in color, and it weighs 127 grams; it is smooth.

The spleen is congested and weighs 7 grams.

The kidneys show marked uric-acid infarction in the medullary pyramids. The ureters and bladder are normal. The adrenals are normal.

The stomach and intestines are normal.

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The brain could not be examined.

Bacteriological Examination.—Smears and cultures from the heart's blood and from the large organs do not contain any bacteria.

Histological Examination.—The alveoli in some parts of the lungs are filled with blood; also the bronchi; the lining epithelium normal. Spleen, adrenals, kidneys, thyroid, and liver greatly congested; most of the alveoli of the thyroid are empty; in some is a pinkish material (hematoxylin and eosin stain). Sections of the mitral valve show no inflammatory changes.

Fig. 3.—Amplified sketch of malformation seen in Fig. 2.

Study of the anomalies of the semilunar valves quickly brings out the unique and peculiar character of the anomaly in this case. Indeed, it is not an anomaly of the aortic valves as much as of the aortic septum. I have found no mention of any similar condition in the literature.[27]

The most common anomalies of the semilunar valves

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are the well-known fenestrations near the free margins, and deviations in number,[28] size and form. Other congenital anomalies are very rare, indeed. Dilg[29] describes a rare and complicated anomaly: right conus stenosis, two pulmonary semilunars, and stenosis of the conus of the left ventricle produced by a peculiar circular endocardial fold partially subdivided into valves, the shallow, valvular sinuses opening toward the ventricle. Dilg regarded this tendinous ring as an imperfect, second row of valves, the condition resembling somewhat that observed in some of the bony fishes in which the conus arteriosus presents several transverse rows of valves.[30]

In Banks'[31] case of "perforation of the aortic valves—loud musical murmurs"—the aortic valves were "cribriform," and there were three little rudimentary valves one-quarter of an inch below the aortic orifice. Corrigan,[32] in a letter to Banks, attributes the musical murmur to the vibrations of the rudimentary valves.

Röhrle[33] describes a tendinous cord in the aorta of a child. This was the only case of the kind in 25,000 autopsies at the Foundlings' Home in Moscow. The tendinous band originated at the left end of the left semilunar valve, and was stretched quite tightly across part of the lumen of the aorta to the left end of the right semilunar valve. The two ends were thin-like threads; the central part was 0.5 mm. in diameter.

Robert S. Archer[34] describes a similar band in a man, aged 39 years. The band was stretched loosely across the lumen of the aorta just above the line of insertion of the aortic valves. It arose by an expansion, one-half inch wide, from the aorta just above the junction of the posterior and left lateral semilunar valves; gradually narrowing, it became inserted at the junction of the posterior and right lateral cusps, thus dividing the area of the vessel into two unequal parts. It seemed to consist of the same kind of tissue as the valves. Otherwise the heart was normal. No clinical observations of the

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heart's sounds were made. Archer believes the development of this band in some way was connected with the development of the valves.

Kretz describes an analogous case in which two fibrous bands crossed the aorta from before backward; one, arising from the right aortic valve, was inserted into the concave side of the aortic arch, 3 cm. above the valves; the other crossed the aorta higher up. These bands are regarded as remnants of the partition between the two embryonic aortæ.

Bouillaud[35] also describes an aortic band or fold, but I have not been able to secure details. Stintzing[36] describes a replacement of one pulmonary segment by two parallel, wholly attached, smooth, narrow bands or ledges extending, one wholly, the other but half way, across the valveless space. Duckworth[37] showed a heart with four semilunar valves. "The adventitious valve . . . communicated with one of its fellows at its insertion by an aperture large enough to admit a crow quill."

There is nothing directly comparable with the anomaly in the present case.

The marked leakage under the base of the anterior valve produced hypertrophy of the heart, especially the left side; it also led to marked dilatation of the arterial duct, and, further, to pulmonary and general venous congestion.

The smoothness of the depression at the aortico-septal junction, the normal condition of the coronary artery arising from its bottom, and the well-formed aortic valves tend to the conclusion that the lesion is the result of purely developmental disturbances rather than of intra-uterine aortitis; but the exact genesis of the anomaly is probably not explainable at this late day. One may say, however, that "as with every other anomaly, adequate knowledge will show it to be a natural sequence."

The exact developmental history of the human semi-

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lunar valves has not been worked out. According to current teaching,[38] four small endothelial cushions appear at the ventricular orifice of the bulbus aortæ before its division into the aorta and pulmonary artery has taken place. Two of these are merely the ends of the ridges by which the aorta is divided (Minot). On completion of the division the two ridges are divided, thus making four protuberances, or in all six—three for each artery. These cushions may be seen in the human embryo of seven weeks (Minot). From them develop, by a process of hollowing out, the semilunar valves.

As already apparent, there is no malformation of the valves proper in this case. The endothelial cushions appear to have developed normally. Possibly the hollowing-out process may have extended to the wall of the aorta, and thus produced the oval depression under the valve, in the same way as Vierordt suggests that communication may be produced between the aorta and the pulmonary artery. It is a little difficult to understand, if this explanation be accepted, how the hollowing-out process could have jumped, as it were, so completely from the valve and out upon the aorta.

We learn further from embryology that the two ridges that divide the primitive aorta extend into the ventricle and help to form the interventricular septum. The aortic septum grows down to the edge of the septum inferius of the ventricle, and thus turns the original interventricular opening into the orifice of the aorta. This is accomplished chiefly by the left or anterior ridge, the right or posterior passing out on the lateral wall of the ventricle, where it is lost. The left ridge, however, runs on to the edge of the septum inferius (Minot). The thinness and the bulging of the aortico-septal junction under the anterior valve may be regarded as indicating a defective development of this part of the aortic septum—the left or anterior ridge. Union with the septum inferius ultimately took place; perhaps the septum

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inferius extended further up than usual; but in the meantime the endothelial cushion forming the anterior valve had extended across the defect. The primary endothelial cushions normally grow out until they meet each other. If there were an opening into the right ventricle at the bottom of the present aortico-septal depression no one would hesitate a moment in interpreting the anomaly as the result of a defective aortic septum. No doubt the depression in this case has greatly enlarged, until somewhat resembling an aneurysm, by the pressure of the direct and regurgitating blood streams that passed under the valve. Looking at the case in this way, one may say that defective aortic septum may lead to communication between the aorta and the pulmonary artery, between the aorta and the right ventricle, and between the aorta and the left ventricle under a semilunar valve.

November 12, 1900.

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TUBERCULOUS PERIMYOCARDITIS WITH TUBERCULOUS AORTIC ANEURYSM IN A DOG.

BY LUDVIG HEKTOEN.

I am indebted to Dr. Donlon for the opportunity to study the following highly interesting case. The clini-

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cal history and postmortem examination are by Dr. Donlon.

The animal was a fine, intelligent bulldog, 8 years old, weighing in health about forty-two pounds, splendidly proportioned, a victorious fighter, displaying in all its encounters more than ordinary strength and endurance. It sprang from a healthy stock.

The present trouble began three years ago; it was first noticed a few days following a short confinement in the dog pound. The dog became mangy, scratched and tore its hide with its teeth, and was soon covered with sores. It rapidly lost flesh, was easily fatigued and rendered breathless; ascites followed. The disease was regarded as of the heart, and thought to follow injury of the breast from kicks while in the dog pound.

The abdomen was tapped, and the dog soon regained its former vigor and so remained for about fifteen months. Then it gradually became emaciated, was persistently attacked by fleas, which caused it to scratch and tear its hide badly. It became breathless on slight exertion; its appetite poor; its legs edematous. This condition continued for about a year, when, after a few days of failure, the dog died.

Postmortem examination was made about eighteen hours after death. Dog, male; weight about twenty-five pounds; poorly nourished. Extremities swollen from edema. Pleural cavities empty and free from adhesions. A depressed scar two inches long was found in the apex of the right lung. The inner anterior borders of both right and left lungs are adherent to the pericardium, from apex almost to base; the adhesions are rather firm, and the lung tissue in the vicinity of the adhesions normal; crepitant throughout; no tubercles present. The bronchial glands are enlarged to the size of a hazelnut and pigmented. The pericardial layers are adherent from base to apex. The adhesions separate with some difficulty, leaving raw surfaces in some places, inter-

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spersed with irregularly shaped firm white masses, which project above the cardiac tissue. The peritoneal sac is empty and normal in appearance. The alimentary canal is normal. The liver is normal. The right kidney is about one and a half times the size of the left, which is apparently atrophied; it contains two small white spots about the size of millet seeds and not unlike tubercles. The testicles are normal. The mesenteric and retroperitoneal glands are normal. The brain and cord were not examined.

The heart was placed in a solution of formalin and eventually brought to my laboratory. A more extended examination of the heart shows the following: The heart measures 8.5 centimeters from base to apex, and transversely in its greatest diameter 7.5 centimeters. The anterior and right lateral surfaces of the heart are covered quite uniformly with nodules, varying in diameter from 0.5 to 2.5 centimeters. Some of them have coalesced, especially those covering the right heart and apex, forming large masses. Two isolated nodules are present on the posterior surface of the right heart, and the right auricular appendix is involved by two separate growths, one located at its apex. The nodules in the heart muscle project above its surface about 2.5 millimeters and are covered by epicardium. On the cut surface the nodules appear lighter in color than the heart muscle and firmer in consistency. They extend to a depth in the heart muscle equal to one-half of its entire thickness. The interior of the heart is normal.

One nodule, about 1.5 centimeters in its greatest vertical diameter, is located at the obtuse angle of the junction of the innominate artery and aorta. It involves the arterial wall and extends about half-way around these vessels. On the cut surface it is shown to be one centimeter thick as an average, the center being thicker than the margins. The cut surface is grayish in color and is clearly distinguishable from the arterial walls, which it

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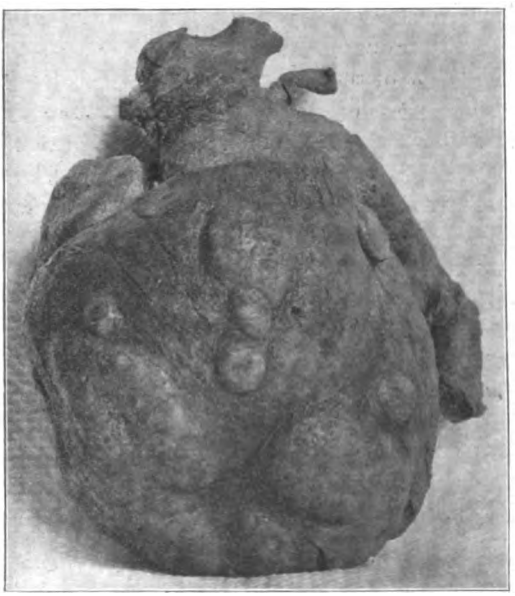
has replaced to some extent. The internal surface is roughly concave and shows a ragged excavation, with the apex directed outward and its base toward the arterial lumen. At the deepest point it is six millimeters. This excavation, or aneurysmal bulging, involves the center of the nodule.

Microscopic sections of the nodules in the heart show an extensive, rather recent, fibrous framework subdividing the nodules into a number of irregular spaces, or



nests, of varying size and outline. The spaces contain accumulations of cells, the central part generally being degenerated and necrotic, the nuclei refusing to stain. In the older necrotic areas the outlines of the cells are wholly lost, a granular detritus remaining. There is much cell infiltration into the fibrous framework of the nodules, and also into the myocardium adjacent. The cells are mostly of the type of the small lymphocytes; there are numerous plasma cells, some endothelioid cells,

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but few polymorphonuclear leucocytes, and no giant cells. There are no typical tubercles anywhere. Numerous sections were stained for tubercle bacilli, and after many trials a few scattered organisms were found among the cells.

Sections of the nodule upon the aorta, cut parallel with the long axis of the aorta, show in the center the excavation mentioned in the foregoing. The main mass of the nodule is of the same structure as the subepicardial nodules, and is situated in the adventitia of the aorta; there are a number of nerves along its external margins. Distinct lymph nodes are not seen. There is extensive necrosis throughout the mass. On carefully examining the various coats of the aorta, at the site of the aneurysmal bulging, in sections stained by Weigert's method for elastic fibers and by the ordinary methods, the following is made out: There is considerable fibrous thickening of the intima about the opening into the aneurysm; there are some areas of infiltration with cells in the interior and at the margins of the fibrous tissue which does not contain any elastic fibers. The most frequent cell form is probably young connective tissue cells, but plasma cells, lymphocytes, and polymorphonuclear leucocytes are present; there are no giant cells; there is more or less necrosis among the cells. As the margins of the aneurysmal opening are approached the fibrous tissue becomes thicker at the same time as it becomes hyaline and anuclear, staining diffusely with eosin, and covered with hyaline thrombotic material which stains brightly red with eosin.

Corresponding to the center of the opening into the aneurysmal cavity there appears to be a complete interruption, for about three to four millimeters, of the intima and the media. This is shown especially well in sections stained by Weigert's elastic fiber method. The margins of the media, and especially of the intima, are turned outward into the little cavity. The media is cut

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across abruptly, as if a piece had been punched out, and the margins are either free or covered with masses of the thrombotic, hyaline material which is found throughout the excavation in the nodule in the adventitia. Some of this thrombotic material fell out during the preparation of the sections. Strands and shreds of elastic tissue are present in the wall immediately below the margins of the defect in the media, and from their arrangement it appears as if they had been carried outward as the wall gave way. Numerous islands of cells are present in the media near the defect; they are most marked in the deeper or external layers of the media, and corresponding to these islands there is a complete absence of the elastic elements. As the shallower parts of the cavity are examined it is found that the media is extensively invaded by granulation tissue, so that the elastic layers are broken up into irregular fragments and masses which have become disarranged. There is more or less marked outward bulging of the media, and in places complete interruption of its continuity has taken place, the elastic elements being apparently broken up and pushed away. Here the thickening of the intima is also usually well marked, covered by hyaline material, and containing inflammatory districts similar to those in the adventitia and the media. In a few places the elastic elements of the media appear to have lost their affinity for Weigert's stain even where there are no inflammatory changes, and irregular patches occur in which the elastic layers appear to be replaced by fibrous tissue, the normal elastic layers passing apparently directly into fibrous bands; but no break in the wall ever occurs at any such place. In the main the reaction to Weigert's stain is typical and decisive.

On staining for tubercle bacilli by means of the carbol-fuchsin method enormous masses of acid-proof bacilli (resisting decolorization for several minutes by 10 per cent. sulphuric acid in water and by 3 per cent. nitric

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acid in absolute alcohol) are seen in the innermost layers of the internal thickening and in the hyaline deposit upon the intima. In order to better study the bacilli, narrow transverse layers were cut, extending across all the coats of the vessel at the margins of the aneurysmal cavity, and embedded in paraffin; sections were then stained and counterstained in various ways after being fixed to the slide. But few organisms are present in the nodule in the adventitia; here they occur singly and only occasionally. In the intimal thickening dense masses are found between and upon the trabeculæ of the connective tissue and of the hyaline thrombus, frequently without any evidence of acute cellular reaction about them, but growing in switches or tresses as if in pure culture, and visible to the naked eye as red patches. Masses are also found between the elastic laminæ of the inner layers of the media and in the cellular areas in the deeper layers. While studying the relations of the bacillary masses to the various layers of the vessel, I made the observation that when the tubercle bacilli are stained with carbol-fuchsin, decolorized by sulphuric acid or Gabbet's solution, stained with acid orcein, washed in alcohol, and cleared in clove oil, they assume a violet or purplish color, which is permanent. This reaction may be worthy of further study.

A lymph node connected with the pericardium shows a fibrous structure, much coal dust, rather hyaline blood vessels, numerous plasma cells, and a few foci of necrosis similar to those in the subepicardial nodules; but no giant cells and no typical tubercles.

No other tissues were examined microscopically.

In regard to tuberculosis in the dog, and to tuberculosis of the canine pericardium in particular, attention may be directed to Sheldon's article,[1] in which is recorded an example of tuberculous pericarditis studied in this laboratory, and to recent reports of similar cases by Petit,[2] and by Petit and Basset.[3]

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The principal point of special interest in the present case is the periaortic nodule and the changes in the wall of the aorta. They call to mind the interesting subject of tuberculosis of the aorta in general, a subject so recently and so fully considered by Blumer[4] in this country, and by Benda[5] in Germany, that there remains for me merely to point out the essential features, and if possible the mode of origin, of the tuberculous aortitis in my case.

Benda was led to study tuberculosis of the aorta in connection with his investigation of the genesis of acute general miliary tuberculosis. This large problem is discussed also by Gaylord in his "Critical Summary of Literature on Tuberculosis of the Walls of the Blood Vessels and the Production of Miliary Tuberculosis,"[6] in which are reviewed the principal events in the development of our knowledge of this subject previous to Benda's work.

Tuberculosis of the aorta may be caused by extension into the aortic wall of extravascular tuberculous foci—for instance, in lymph nodes, as shown in the cases described by Dittrich[7] and Kamen.[7] In Dittrich's case numerous bacilli were present in the aortic wall which contained tubercles. In Kamen's case dilatation and rupture of the aorta had occurred at the point of adhesion to the gland. Bacilli were not found in the aortic wall, which was tuberculous and arteriosclerotic. In Sigg's case the tuberculous lung, containing a cavity, was adherent to an aortic aneurysm which bulged into the tuberculous cavity; the wall of the aneurysm was perforated, but the opening was covered externally by the caseous contents of the cavity and internally by a thrombus; the aneurysmal wall was tuberculous, and many bacilli were present even in he thrombus. Buttermilch[9] describes tuberculosis of the aorta as due to extension from tuberculous focus of the vertebræ.

Petit and Basset[10] describe a hemorrhagic pericarditis

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in a dog with general tuberculosis of the lungs, peribronchial lymph nodes, liver, and kidneys. In a mass of tuberculous glands at the tracheal bifurcation was a cavity filled with blood, and in communication with the lumen of the aorta, the wall of which had been perforated by a progressive caseation. The tuberculous generalization was traced to this rupture of the aorta.

This group of cases are all samples of what Benda calls tuberculous periangitis—that is, periaortitis—which as in other vessels may extend clear through the vessel wall. The inner aspect of the lesion may be covered by thrombotic deposits in which bacilli proliferate freely.

But tuberculosis of the aorta may also result from the implantation of tubercle bacilli upon the healthy or the sclerotic intima, or from their lodgment in an existing thrombus. It is seen that in respect to genesis and other features aortic tuberculosis corresponds well to tuberculosis of other vessels, including the thoracic duct and also the heart.

Recent more or less distinctly miliary tuberculosis of the aorta is mentioned by Weigert in his epochal studies on acute miliary tuberculosis, and typical examples are more fully described by Schuchardt,[11] Flexner,[12] Hanot,[11] Hanot and Lévy,[11] Blumer,[12] who records two instances. In all these cases there existed a general miliary tuberculosis; the structure of the aortic lesion, usually not over a pin's head in size, was that of small aggregations of cells or of more or less distinct miliary tubercles, usually with some caseation, and containing now few, now innumerable bacilli. Generally these nodules appear as if placed directly upon the intima, the cell infiltration not extending below the inner elastic layer. In one of Blumer's cases there were three separate nodules of this kind upon the intima of the abdominal aorta, which in general seems to have been involved

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nearly as frequently as the thoracic. Arteriosclerosis may be absent or present.

It is probable that the further growth of the intimal tubercles, associated with more or less thrombotic deposits, gives rise to the larger, more polypoid tuberculous formations, with irregular, nodular, though smooth surface, and sometimes several centimeters long, described in the aorta by Hanot,[13] Stroebe,[14] Benda,[15] Aschoff,[16] and Longcope.[17] (Longcope's report reached me after this article had been put in type). These cases were all undoubtedly of endaortic origin. In Aschoff's case the polypoid outgrowth is described as bean-sized, attached by one end to a sclerotic area in the aorta, and as resembling much a white thrombus. These foci present the same results of the molding of the current as thrombi. It may consequently be difficult to recognize these foci as tuberculous from the naked-eye appearances; and this is also true of the smaller miliary growths. All the instances of polypoid aortic intimal tuberculosis seem to have developed upon sclerotic areas. Besides typical tubercles with giant cells, these growths also present distinct caseous foci, sometimes wholly liquefied, and on the free surface are layers of trabeculated, hyaline, thrombotic material. Tubercle bacilli in enormous numbers were present in all the nodules of this kind that have been described. Both Benda (who described two different cases, one being regarded as a tuberculous metastasis in a thrombus) and Aschoff lay special stress upon this fact. In their cases the bacillary areas were readily visible to the naked eye in the stained specimens, and microscopically the arrangement in tresses as seen in growths of the tubercle bacillus upon artificial media ("Kulturzöpfe") was noted. Colossal masses of bacilli may be present in the thrombotic layers directly under the blood stream; the surface of the nodule may be glistening and smooth, yet the blood current may be in direct contact with the bacillary masses—hence the importance of such

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endovascular foci in the development of miliary tuberculosis. Indeed, it seems that the larger endovascular foci present exceptionally favorable conditions for the growth of tubercle bacilli. This has been noted also in polypoid tuberculous endophlebitis and in tuberculous endocarditis. The thrombotic deposits, at first fibrinous, later trabeculated and homogeneous, serve as an excellent culture medium for the bacilli, which grow luxuriantly into the material in the same manner as on artificial media. This is shown well in my case, the thrombotic deposits about the opening of the aneurysmal bulging containing great heaps of bacilli. On account of the great multiplication of bacilli in the endovascular tuberculous formations and its significance in the etiology of general miliary tuberculosis, Benda appropriately designates them as breeding places ("anreicherungstätte").

With this brief summary of aortic tuberculosis before us, it is seen that the lesion of the dog's aorta corresponds most closely to the case described by Kamen of extension to the aorta of tuberculosis in a lymph gland, with subsequent aortic dilatation and rupture. Whether the lesion in the dog's heart is primarily periaortic or endaortic it is now probably not possible to determine definitely. Perhaps it is more reasonable on the whole to regard it as the result of extension from without, the periaortic focus being a result of the tuberculous infection of the pericardium. We have learned from the case described by Sigg that tubercle bacilli may proliferate freely in the endovascular deposits even though the invasion occurs not from the blood but from without. Hauser[18] and Kossel[19] show this to be true also in perivascular tuberculosis extending to the cranial sinuses. Hence the vastly greater number of bacilli in the innermost parts of the aortic lesion as compared with the perivascular portion does not necessarily mean that the extension is from within outward. Benda also recognizes the fact that the number of bacilli in the inner layers

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of an endovascular tuberculous lesion due to extension from without may be quite as great as in the primarily endovascular, polypoid tuberculosis. Indeed, it seems quite probable that it is the character of the substratum, especially the fibrinous material, that largely determines the production of such large masses of bacilli in these foci rather than the direction from which localization takes place.

On the other hand, there is no decisive evidence that could positively exclude the possibly primarily hematogenous nature of the aortic lesion. It even might be claimed with some show of reason that the pericardium became infected from the aortic focus. As shown by Weigert and by Benda an endovascular focus of this character precedes the development of general miliary tuberculosis, and consequently it may exist without necessarily being associated with the general miliary disease. As taught at present, hematogenous polypoid tuberculous endangitis results from the implantation upon the intima of a few bacilli entering the circulation directly or indirectly from some local area; this is succeeded by a massive proliferation of bacilli in the resulting nodule, which eventually becomes the center of dissemination for the bacillary hosts causing the general tuberculosis. Hence the lesion in the dog's aorta may have resulted from a primary endangitis even though there was no miliary tuberculosis. It might at any time have become the source of a general tuberculous eruption; but the animal died without any explosive distribution taking place, as far as can be told from the appearance of the organs after death.

The possibility that the aortic lesion might have resulted through the vasa vasorum should be mentioned. As far as I can see there is not any special point of evidence to be urged for or against this possibility.

At all events the tuberculous granulation tissue caused the elastic fibers and layers of the media to melt away.

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and perforation and aneurysmal bulging to take place. This aneurysm may be compared with the erosion aneurysms that develop so frequently upon the branches of the pulmonary arteries coursing through tuberculous cavities. In this case the tuberculosis would be regarded as beginning in the adventitia and extending to the media and intima. I have called attention already to the similarity between Kamen's case and my own. Or the aneurysm may be compared with the mycotic or embolic aneurysms observed in the brain as well as elsewhere. In this case the tuberculous infection would have to be regarded as primary upon the intima—a metestatic intimal tuberculosis with destruction of the walls of the aorta and the formation of an aneurysm. Benda describes and figures[20] several spindle-shaped tuberculous aneurysms of the thoracic duct caused by polypoid tuberculous endangitis; in these the media and adventitia remained intact. In tuberculous leptomeningitis I have seen a caseous intimal focus cause perforation of the elastic layer, the ends of which were bent outward, there being some infiltration of the media and the adventitia, the whole picture resembling a small aneurysm.[21]

In concluding it may be said that a tuberculous invasion of the aorta caused perforation of the wall and aneurysmal bulging; that the tuberculosis probably invaded the wall from without, but that a primary tuberculous endangitis can not be excluded positively; and that the inner layers of the intimal thickening, due partly to proliferation, partly to hyaline thrombosis, contain tubercle bacilli in enormous numbers. but that a miliary tuberculosis did not exist, although the conditions for its development at any moment were quite well established.

February 12, 1900.

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21. See Fig. 5, plate vii, Journal of Experimental Medicine, 1896, i.

REPORT OF A CASE IN WHICH THERE WERE TWO PARIETAL DISSECTING ANEURYSMS (VESTBERG) IN THE SAME HEART.

E. R. LE COUNT.

Dissecting aneurysms of the heart are those in which the aneurysmal cavity is formed, in part at least, by the splitting force of the blood pressed into it by the heart's contraction.

A. Vestberg, from a careful study of the anatomy and a painstaking examination of the cases that have been reported, has divided them into four varieties: *Septal,* aneurysms of the septa; *parietal,* those occurring between the layers of the myocardium; *valvular,* occurring in the valves, and *interparietal,* those formed between the external surfaces of the heart that are normally united by loose fibrous tissue. The last form is the most frequent; of 59 cases Vestberg found that 47 were inter-

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parietal and that most of these occurred in the connective tissue about the root of the aorta—the periaortic space.

ABSTRACT OF CLINICAL HISTORY.

Frank L. entered the Cook County Hospital during the service of Dr. Butler, June 23, 1899.

Previous Illnesses.—Gonorrhea in 1879; no history of syphilis; tuberculous glands were removed from the neck in 1885.

Family History.—Negative.

Present Illness.—Four days previous to the date of entrance he was taken suddenly ill with severe vomiting and attacks of coughing which, in several instances, terminated in the expectoration of considerable blood These attacks were accompanied by dizziness and ringing in the ears. Respiration became more difficult each day and the feet began to swell. Severe thirst was experienced, but drinking was followed by vomiting.

Examination on Date of Entrance.—There is a marked dyspnea; the respiration excursion and expansion are slight; a heavy impulse can be seen in the precordial region; there is normal resonance over the entire chest.

Heart.—Relative dulness extends upward to the third rib, on the right side to 1½ inches beyond the right border of the sternum. The apex-beat is in the sixth interspace 1½ inches to the left of the nipple line; it is heaving in character and plainly visible. A loud, blowing systolic murmur is apparent on auscultation; it is heard most plainly at the apex and is transmitted to the left. The second pulmonic sign is accentuated. On palpation there is a marked thrill. Below the zyphoid is heard a loud systolic murmur; there is also a distinct pulsation which is expansile in this region, and a palpable thrill.

The upper border of hepatic dulness is at the fourth rib in the sternal line, and the seventh rib in the mid-

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axillary line; its lower border is one hand's breadth below the costal arch. There is marked hepatic pulsation.

On the day of entrance 600 c.c. of blood were withdrawn from his arm.

June 26: Complains of severe epigastric pain.

June 27: Fine crepitant râles are heard over the right lower lobe behind; they are only present with deep inspiration. Diminished resonance and lessened respiratory sounds are also present here. The apex-beat is in the sixth interspace in the anterior axillary line. There is edema of the right hand.

July 9: Drinking is followed by vomiting.

July 16: The patient was seized with a sudden severe pain in the right side of the chest; this was followed by the expectoration of clots of blood. Over the right lung, between the nipple and the border of the sternum, there is an area two inches in diameter over which the breathing is bronchial; there is no increased dulness here, but voice sounds are more intense than normal. Over the lower left lobe behind numerous small, moist râles can be heard.

The urine examined July 7 yielded the following data: Color, deep amber; reaction, alkaline; sp. gr., 1028; albumin present; no sugar. Microscopic—Many dark, coarsely granular and a few hyaline casts.

Death occurred August 3.

ANATOMICAL DIAGNOSIS.

Aneurysms of the heart.
Fibrous pericarditis.
Hemorrhagic infarcts of both lungs.
Marginal emphysema.
Passive hyperemia of liver, kidneys and spleen.
Anasarca.
Diphtheric colitis.
Old umbilical hernia.
Cervical cicatrices with keloid formation.

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Heart.—Weighs slightly over 1000 grams. It is 17.5 cm. in length and at its greatest breadth 13 cm.; it is 9 cm. thick. The aortic and pulmonary valves are competent to the water test. The apex is made up mainly of the left ventricle.

The right auricle contains considerable clotted blood. The tricuspid orifice easily admits the tips of five fingers.

The left auricle is enormously distended; its wall measures 3 mm. in thickness, in certain places 4 and even 5 mm.; the lining is firm, whiter than normal and thickened; the openings of the pulmonary veins are surrounded by thickened endocardium. The foramen ovale is closed by a firm membrane. The left auricular appendage appears small; its greatest diameter is 2 cm. The wall of the right auricle is thickened in places by heavy muscular trabeculæ and at such places the wall is 1 cm. in thickness. The lining is firm and white.

The right ventricle is 10.5 cm. long; its wall measures 4 to 7 mm. Its lining shows no changes. There are no changes in the pulmonary cusps nor in the tricuspid leaflets. The aortic valves—more especially the anterior and posterior cusps—are fenestrated by a few openings which are horizontally directed; they all occur above the lines of contact of the cusps; the largest of these openings measures 5 mm. in length.

The cavity of the left ventricle measures 9 cm. in length; its walls average 1.5 cm. in thickness. At its point of greatest thickness the wall measures 2 cm. In this cavity are numerous aberrant chordæ tendineæ. The free margin of both mitral curtains is thickened and the chordæ tendinæ are much shortened; some barely measure 1 cm. The papillary muscles are much heavier than usual. At the point where the interventricular septum joins the posterior wall of the left ventricle, at the upper part of the cavity of this ventricle, just below the attachment of the anterior mitral leaflet to the heart wall and leading from the cavity of the left ventricle are two

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openings separated from one another by a firm band which is covered by white or ivory-colored endocardium and which measures 3 to 4 mm. in width. The endocardium around the openings is thickened and pale; it forms a white collar 1 cm. wide. These openings are placed side by side; the anterior is the larger; it is oval and measures in its longest diameter 16 mm. The posterior opening is also oval; its longest diameter measures 11 mm. The anterior opening leads into a cavity which would easily contain a goose egg; it is entirely closed save for this opening. This cavity measures 9.5 cm. in its longest diameter, which is vertical (with the heart on its apex), 5.5 cm. in its longest transverse diameter measured on its inner or visceral wall, and 3.5 cm. from its inner to its outer wall. The lowermost point of this cavity is 6.5 cm. from the apex of the heart; its topmost limit is on a level with the highest point of the external surface of the heart. Its inner wall is made up, for the main part, of the anterior wall of the right auricle and its appendage; the lower one-third or one-fourth of its inner wall is formed by the upper part of the wall of the right ventricle—that part which normally rests on the diaphragm—and a part of the septum between the ventricles.

The posterior of the two openings in the left ventricle opens into a smaller cavity, which is quite spherical in shape and averages 2.5 cm. in diameter. This cavity is situated entirely within the wall of the left ventricle at its upper posterior angle. The outer wall of this small cavity consists of 6 mm. of heart muscle to which the pericardium is adherent externally; its inner wall at one point is translucent, but firm and fibrous; at this point the cavity of the small aneurysm is separated from the cavity of the left auricle by a membrane which measures 2 mm. At another point the inner wall of the small aneurysm is separated by firm fibrous tissue from the passageway connecting the large aneurysm with the left

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auricle; the firm fibrous separation is 3 to 4 mm. in thickness at this point.

Both cavities contain laminated clots of blood, but in the larger cavity the blood is, for the greater part, dark and semi-fluid. Externally the heart is covered with an adherent pericardium. Both coronary vessels possess a few raised, yellowish areas which are widely scattered. The left coronary is slightly constricted at its point of entrance into the aorta. Both vessels, when opened as far as the apex, show no occlusions.

Microscopic Examination.—In sections from the wall of the left ventricle and in sections from one of the muscular ridges in the wall of the right auricle, the muscle fibers appear larger and heavier than normal; their nuclei show the divers forms and sizes so often met with in heart muscle cells, many are block-like rectangular masses of chromatin with apparently no nuclear membrane surrounding them. The muscle fibers average twice the width of the nuclei; the cross markings are distinct; there is a little brown pigment at the poles of the nuclei. There are no changes in the smaller branches of the coronary vessels, nor is there any increased amount of connective tissue evident.

Sections of the upper part of the wall of the large aneurysm show many large bands that are similar to the heavy fibers met with in keloids. They stain red with Van Gieson's stain, possess fine longitudinal markings as though made of finer fibrillæ, possess no nuclei and are slightly wavy in arrangement. These heavy fibers are not of uniform size, some being much larger than others; between them occur occasional spindle-shaped nuclei that belong to small cells. There are also many heavy elastic fibers between these bands (Weigert's stain, used without heat). More internally toward the lining of the aneurysm are short spindle-shaped cells with large nuclei that resemble the nuclei of heart muscle fibers; these cells are not numerous, but form a narrow zone.

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More internally is a layer of fibrin that becomes less dense as the surface is approached. In this wall are numerous small blood vessels.

Sections cut from the outer wall of the large cavity show a very similar structure; there are perhaps fewer vessels. There are no fibers of elastic tissue here. Sections cut at right angles from the cavity into the wall of the small aneurysm have upon the lining edge fibrin; external to this is a considerable zone of fibro-cellular structure with scattered minute elastic tissue fibers. This encapsulating connective tissue is most cellular externally; here occur many typical plasma cells about the small blood vessels that are quite numerous (polychrome blue—Unna). The blood vessels resemble those of granulation tissue.

There are very cogent reasons for considering these cavities as dissecting aneurysms. The main reason is their location so contiguous to the mitral valve, in a position where an acute valvular endocarditis might readily give rise to mural implantations by contact; indeed, the very existence of two aneurysms with openings so close together speaks for such an etiology.

Although there remains no method of determining to what extent the heart walls were "dissected" by the blood pressure to form the cavities of the aneurysms, it is difficult to believe, if we admit their etiology in an acute process, that pressure did not act some rôle in the enlargement that occurred previous to healing.

As for their origin in a chronic fibrous myocarditis that produced localized points of weakness; the absence of marked changes in the coronary arteries and of any increase in the interstitial tissue of the myocardium are opposed to such a view. Infarcts occur more frequently in other parts of the myocardium, and if multiple infarcts should heal and give rise to aneurysms there is small likelihood that two such aneurysms would be produced as these. For these reasons it seems proper to

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conclude that these cavities connecting with the left ventricle originated in an acute process that caused two weak points in the wall by degeneration or necrosis of the muscle (or both); that the destruction of muscle fibers and blood pressure caused dilatations in which, however, the inflammation healed; that subsequently the blood pressure greatly enlarged one of the aneurysms.

October 12, 1899.

THE DISTRIBUTION OF SEGMENTATION AND FRAGMENTATION IN THE MYOCARDIUM.

WILLIAM B. WHERRY.

It is generally believed that segmentation occurs most frequently in the left papillary muscle. In cases of marked segmentation throughout the left ventricle, the right ventricle is also, as a rule, involved. It occurs but rarely in the auricles (Hektoen).

The marked frequency with which the papillary muscle is involved is attributed to the absence of diagonal fibers (Israel).

A. Streckeisen[1] in an investigation of one hundred and fifty cases of death by violence states that segmentation occurred most frequently in the papillary muscles or wall of the left ventricle; then in the septum and papillary muscles and trabeculæ of the right ventricle. The auricles are never affected.

At the suggestion of Professor Hektoen the following piece of work was undertaken:

Twenty hearts were preserved in 5 per cent. formalin.

1. Zeigler's Beitrage, 1899, xxvi, 105-131.

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Eighteen pieces were cut from each heart, each cube of tissue being removed from a definite locality and kept in a separate bottle until mounted. The celloidin method was employed; sections were stained with hematoxylin and eosin and mounted in a definite series. In removing the tissue a sharp knife was used and a flat surface of the block was made to correspond with the long axis of the fibers. In order that sections from the various hearts might come from very nearly the same locality, the following scheme was employed:

RIGHT AURICLE.

Sec. 1. (1.) Musculæ pectinatæ at junction of auricular appendix with auricular wall.

Sec. 2. (2.) Posterior edge of tricuspid opening—section parallel to length of opening.

Sec. 3. (3.) Lower border of foramen ovale.

LEFT AURICLE.

Sec. 4. (1.) Musculæ pectinatæ at junction of auricular appendix with auricular wall.

Sec. 5. (2.) Posterior edge of tricuspid opening—section parallel to length of opening.

Sec. 6. (3.) Lower border of foramen ovale.

RIGHT VENTRICLE.

Sec. 7. (1.) Anterior papillary muscle.

Sec. 8. (2.) Right papillary muscle.

Sec. 9. (3.) Posterior papillary muscle.

Sec. 10. (4.) Anterior wall near apex (outside).

Sec. 11. (5.) Anterior wall near tricuspid opening (inside).

Sec. 12. (6.) Interventricular septum.

LEFT VENTRICLE.

Sec. 13. (1.) Anterior papillary muscle.

Sec. 14. (2.) Posterior papillary muscle.

Sec. 15. (3.) Anterior surface of apex opposite interventricular septum.

Sec. 16. (4.) Posterior surface of apex opposite apex of ventricular cavity (outside).

Sec. 17. (5.) Middle of lateral wall of ventricle (outside).

Sec. 18. (6.) Interventricular septum.

In order that the findings might correspond with the generally recognized forms of fragmentation, the divisions made by J. B. MacCallum[2] were adopted, i. e.:

2. Jour. of Exper. Med., 1899, iv. 405-424.

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Number of Heart.	Degenerative Fragmentation and Segmentation.		Right Ventricle.		Left Ventricle.		Amount of Segmentation in Papillary Muscles.
	Right Auricle.	Left Auricle.	Simple Segmentation.	Degenerative Fragmentation and Segmentation.	Simple Segmentation.	Degenerative Fragmentation and Segmentation.	
862	. . . .	6	7, 8, 9, 10, 11, 12	. . . . .	13, 14, 15, 16, 17, 18	. . . . .	Diffuse with diastasis
869	. . . .	. . . .	7, 8	8	13, 14, 16, 17, 18	. . . . .	
874	. . . .	. . . .	. . . . .	. . . . .	13, 15	14, 17, 18	
876	. . . .	. . . .	7, 8, 9	8, 9	13, 14	13, 14, 17	Diffuse with diastasis
879	. . . .	. . . .	. . . . .	7, 8, 11	. . . . .	13. 14, 15, 16, 17	Diffuse.
881	. . . .	. . . .	. . . . .	. . . . .	13, 14, 16, 17, 18	13, 14, 17, 18	
882	. . . .	. . . .	. . . . .	7, 8, 9, 12	13, 14	17, 18	Diffuse, with diastasis and displacement.
888	.	. . . .	8, 9, 11	7, 8, 9	13	14, 16, 17	As above.
889	. . .	. .	8	. . . . .	13, 14, 15	16, 17	As above.
894	. .	. . . .	10	9, 10	13, 14, 17, 18	18	
899	. . . .	6	. . . . .	. . . .	. . . . .	. . . . .	
901	. . . .	. .	. . . . .	12	13, 14, 17	16	
902	. . . .	. . . .	7, 8	7, 11, 12	13, 14, 16, 17	18	As above.
908	. . .	. . . .	9	. . . . .	13, 14, 17	17	
927	. . . .	. .	. . . . .	. . . . .	14	13, 14	
943	. . . .		. . . .	7, 8	13, 14	13, 14, 17	

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In simple segmentation the break is clear-cut and passes through the intercellular cement substance.

In degenerative fragmentation and segmentation the line of cleavage is not clearly marked, may pass through the cement line or through the cell body, and is always the result of sarcolytic degeneration.

Results: No segmentation or fragmentation was found in four cases. The distribution as it occurred in the remaining sixteen cases is shown in the table herewith.

SUMMARY.

Thus degenerative fragmentation and segmentation occurred twice in the left auricle at the lower border of the foramen ovale—one heart showing segmentation throughout the right and left ventricles, and the other showing no other segmentation.

In the right ventricle segmentation occurred in twelve cases and was always associated with segmentation in the left ventricle.

Frequency of distribution:

Papillary muscles, 11 cases.

Interventricular septum, 4 cases.

Inside of anterior wall, 4 cases.

Outside of anterior wall, 2 cases.

Simple segmentation, and degenerative fragmentation and segmentation occurred with about equal frequency in the papillary muscles, and practically corresponding changes were found in the other parts of the ventricle, *e. g.*, where the right papillary muscle showed simple segmentation, the other areas in the right ventricle showed simple segmentation, or this combined with slight fragmentation.

In the left ventricle segmentation occurred in fifteen cases.

Frequency of distribution:

Papillary muscles, 15 cases.

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Anterior surface of apex, 4 cases.

Posterior surface of apex, 8 cases.

Lateral wall, 14 cases.

Interventricular septum, 7 cases.

Here, as in the right ventricle, simple segmentation, and degenerative fragmentation and segmentation occurred with about equal frequency in the papillary muscles, and practically corresponding changes occurred in other parts of the ventricle, excepting at the middle of the lateral wall (outside) where degenerative fragmentation and segmentation, or this combined with simple segmentation, occurred irrespective of the kind of change in the papillary muscles.

In only one case (862) did simple segmentation occur throughout the right and left ventricles.

"Diffuse" segmentation of both left papillary muscles, accompanied by diastasis and displacement of the segments, seems to indicate more or less general segmentation and fragmentation throughout the ventricles.

In cases showing "focal" segmentation of only one or both left papillary muscles, such widely diffused segmentation does not occur.

The ages of the patients varied from 22 to 69 years.

An attempt to associate general segmentation and fragmentation of the ventricles with other disturbances of the cardio-vascular system gave the following results:

Two cases (862, 879) with valvular disease followed by hypertrophy and dilatation of the heart.

Three cases (876, 888, 902) with sclerosis of coronaries and aorta.

Two cases (889, 882) with acute and chronic myocarditis respectively.

June 10, 1901.

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BICUSPID AORTIC VALVES.

H. G. WELLS.

The heart was obtained from the body of a man, 50 years of age, who died of lobar pneumonia. During life there were no evidences of valvular lesions. The right and left aortic semilunar cusps were fused, forming a single large valve, but in the center of this double valve there remains a fold of tissue which represents in a rudimentary form the normal attachment of adjacent valves. This fold is sclerotic and calcified. The two sinuses of Valsalva behind this double valve form a single large pocket, from which the posterior coronary artery arises to the right of the center. At this point the circumference of the aorta is 11 cm., while further on it is but 6.5 cm. The anterior leaflet, which meets this fused cusp so as to be perfectly competent to the water test, is greatly enlarged, so that it is fully as large as the double cusp. Calcareous plaques are found in both cusps.

January 14, 1901.

HENRY F. LEWIS presented two hearts from new-born children with patent ductus arteriosus.

February 12, 1900.

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THE DIGESTIVE SYSTEM.

FALSE DIVERTICULA OF THE INTESTINE.

MARTIN H. FISCHER.

Diverticula of the intestine may be divided into the true and the false. By a true diverticulum is understood one the walls of which are composed of the entire thickness of the intestine; the false diverticulum, on the other hand, is a hernia of the mucosa and submucosa through the muscular wall (von Rokitansky,[1] Leichtenstern,[2] Birch-Hirschfeld,[3] Orth,[3a] Hansemann,[4] and others). Therefore, while a true diverticulum presents all three coats of the gut, a false diverticulum is formed of mucosa and serosa only, with intervening connective tissue. It is further desirable to differentiate between congenital and acquired diverticula. This distinction, however, does not apply to false diverticula, as, so far as known, all of these are acquired, no case of congenital false diverticulum of the intestine having ever been described.

Edel[5] and others would make synonymous the terms congenital diverticula and true diverticula, likewise the terms acquired diverticula and false diverticula, specifying that the former have all three coats of the intestinal wall, while the latter show only mucosa and serosa. The difficulty in determining definitely in many cases whether the sacculation is congenital or acquired, makes this classification objectionable. A definition based upon morphological rather than developmental conditions, though less desirable, is at least a safe one. Furthermore, Edel's definition does not hold good in all instances, as cases of acquired diverticula possessing all

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coats of the intestine have repeatedly been reported. Thus Fiedler[6] records such cases. Wallmann[7] has described nine true acquired diverticula of the large intestine. Norman Moore[8] has reported a case of multiple diverticula of the small intestine in a man 40 years old. The diverticula occurred at the mesenteric attachment of the gut, and were composed of all coats of the intestine. Moore does not state whether he regarded the diverticula as congenital or acquired.

By far the greater number of true intestinal diverticula of congenital origin are the Meckel diverticula, which are formed by a persistence of the omphalomesenteric duct. Other factors may, however, give rise to such diverticula. Grawitz[9] has found a diverticulum of the large intestine whose origin could be traced to fetal malformation. Buchwald with Janicke[10] has described a true diverticulum of congenital origin in the jejunum of a boy 6 years old.

Hansemann,[4] Neumann,[11] and Nauwerck[12] have each reported a case of true intestinal diverticula with accessory pancreas at their apices. Hansemann's case was of a diverticulum at the upper end of the jejunum of a boy 14 years of age. Neumann found a true diverticulum with a pea-sized accessory pancreas at its apex, a case similar to that of Zenker,[13] who found, 54 cm. above the ileocecal valve, a diverticulum at the apex of which was a cherry-sized pancreas. Nauwerck's diverticulum came from the ileum of a man 43 years old and possessed a separate mesentery. Except Zenker, who interprets his case as one of true Meckel's diverticulum, the observers all attribute the occurrence of the intestinal sacculations to traction brought about by the accessory pancreas. Other instances, in which traction has been believed to be the causative agent, have been described by Birch-Hirschfeld.[14] These were caused by connective-tissue bands in the mesentery. In two cases described by Hansemann,[4] a tumor produced the traction.

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The first description of false diverticula of the intestine is usually attributed to Sömmering[37] in his translation into German of Matthew Baillie's "Morbid Anatomy" (1794), but Voigtel[38] cites previous cases recorded by Schröck, Riolan, Günz, Morgagni and Haller, at least some of which undoubtedly belong to this class. The subject is considered in the text-books on pathological anatomy of Cruveilhier, Rokitansky,[15] Förster,[33] Orth,[34] and others.

Fleischmann[16] described in 1815 a false diverticulum of the duodenum. Roth[17] in 1872 gave a critical summary of the cases of duodenal diverticula reported up to his time, and described five personal observations. He came to the following conclusions: Diverticula of the duodenum are exclusively of the false variety; usually only one or two, less frequently three or four are present; they do not become larger than a pigeon's egg, and are usually empty; they occur most commonly at the inner, posterior aspect of the pars descendens duodeni at the entrance of the biliary and pancreatic ducts.

Wallmann[7] found in a part of the small intestine, 48 cm. long, thirty-seven diverticula, of which thirty were said to be between the folds of the mesentery. The diverticula were false, the walls being composed only of the mucosa and serosa. Birch-Hirschfeld[8] has described a case in which the ileum through almost its entire length showed many false diverticula along the mesenteric border. Klebs[18] found in the small intestine of an old man twenty diverticula, varying in size from a pea to a walnut, and all situated within the mesentery. Bristowe[19] found just above the ileocecal valve a solitary diverticulum, the walls of which were formed of mucosa and serosa.

False diverticula of the large intestine have repeatedly been described. Gross[20] described and pictured this condition. Bristowe reported a case of diverticula of the large bowel occurring in a woman 69 years old. The

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walls of the sacculations were formed of mucosa and serosa only. The diverticula were limited to the site of the appendices epiploicæ, and varied in size from a pin's head to a marble. Alibert found 200 diverticula in a colon, while other instances of false diverticula of the large intestine have been described by Schröder, Sidney Jones, Astley Cooper, and others.

All writers, with the exception of Förster,* agree that the false diverticula of the small intestine occur almost exclusively on the concave side of the gut, and that they lie between or close to the layers of the mesentery. Their average size varies from that of a pea to that of a pigeon's egg, but Virchow[21] has shown a specimen in which the diverticula attained the size of a hen's egg.

The etiology of false diverticula is still somewhat obscure. Reference has been made to the production of diverticula by traction; this, however, is not generally believed to be the usual case. It was for a long time held that they were due to increased intra-intestinal pressure of various kinds, as from feces, or gas. Klebs[22] was the first to point out that a certain relation exists between the blood vessels and the diverticula. In his case already cited, the small sacs were true, the larger, false diverticula, and all were at the points of entrance of the mesenteric vessels. This condition led Klebs to the suggestion that either through the growth of the mesentery in length outstripping that of the blood vessels, or more probably through traction in later life upon the mesentery by the intestine, the funnel-like attachment of the intestinal wall to the entering mesenteric vessels becomes converted into a diverticulum. In support of the latter supposition is the greater frequency of these multiple diverticula in elderly and obese persons.

While Good[23] and Hanau,[24] and Hansemann[4] confirm

* As suggested by Hansemann, Förster's apparently exceptional position may be the result of a typographical error, as his description otherwise corresponds to that usually accepted.

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Klebs' observation concerning the relationship of false diverticula of the small intestine to the blood vessels, they attribute the origin of the diverticula to pulsion rather than to traction, and Hansemann has defined more precisely the vascular relationship. Intestinal diverticula occur in those who at no time have given indications of any notable deposit of fat in the mesentery. In a case reported by Hansemann the patient, who died of pneumonia, was 85 years old and emaciated, having always been thin. About 400 diverticula, varying in size from a millet-seed to a pigeon's egg, were counted, the larger number being in the jejunum and upper part of the ileum. There were some, however, in the duodenum and many in the sigmoid flexure, but none in the vermiform appendix or colon. Those in the small intestine were mostly empty, but some of those in the large intestine contained feces. Most of the diverticula occurred close to the mesenteric border, but not actually between the layers of the mesentery. Some in the large bowel were on the convex side of the gut. An interesting relation existed between the diverticula situated at the mesenteric border and the blood vessels; the vessels branched out in the diverticular walls, those beneath the serous surface being arteries, while those visible from the mucous surface were veins. The diverticula had no muscular tunic. The fact that the mucosal hernias were not separated from their corresponding veins led Hansemann to conclude that the false diverticula were formed by the bulging of the mucosa through the muscularis along the sheaths of veins passing from the intestine into the mesentery.

Heschl,[25] in 1880, showed that the intestine ruptures under pressure at the points where the diverticula are found. Good, working under Hanau's direction, by filling a loop of intestine with water and subjecting it to hydraulic pressure, was able to produce trench-like furrows along its mesenteric border before perforation oc-

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curred. Hansemann was more successful, as he was able bv a similar procedure to produce in the small intestine sacculations which were far more typical than any pro duced by previous experimenters, and to demonstrate that these bore the same relation to the veins as the false diverticula observed in his patient.

Senility doubtless favors the formation of intestinal diverticula, as this lesion is very rarely found in young persons. Hansemann's attempts to produce diverticula experimentally succeeded when senile intestines were employed, but failed entirely with the intestines of children.

Besides the normal loci minoris resistentiæ, other etiological conditions are to be considered. Abnormally great intra-intestinal pressure loses some of its importance as a causative agent when it is remembered how rarely postmortem examination reveals diverticula of intestines in which such pressure has undoubtedly been present. Chronic constipation may be considered as a predisposing factor, especially in those true diverticula of the colon which represent scarcely more than a dilatation or exaggeration of the normal haustra coli, but here also there is marked discrepancy between the frequency of habitual constipation and the occurrence of diverticula.

Fleischmann pointed out that the muscular fibers of the duodenum are normally separated by the common bile duct, thus furnishing a condition favorable to the formation of a diverticulum in this part of the duodenum. Roth mentioned fatty degeneration of the muscularis as a possible cause. A stenosis, leading to increased intestinal pressure, may be produced by large gallstones retained within the intestine. Instances of diverticula from this cause are cited by Leichtenstern.[2] A retention cyst of the appendix may lead to the production of diverticula in it (Kelynack,[26] Ribbert[27]). Finally, attention may be called to the influence, predisposing to

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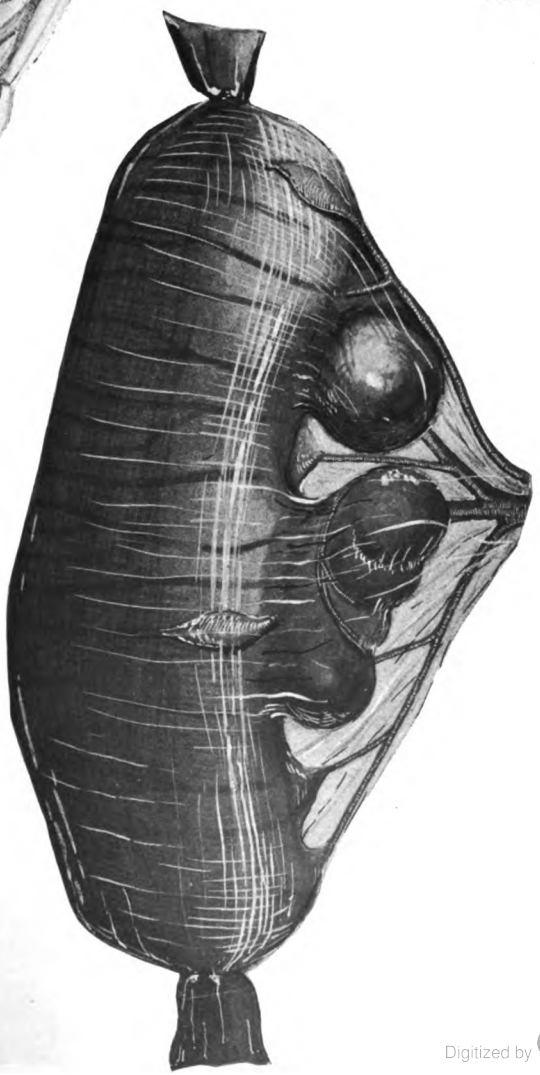
FIG. 1.

FIG. 2.



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diverticular formations, of general sluggishness of the intestinal functions, due to marasmus, phthisis, or carcinoma.

The existence of intestinal diverticula is usually unattended by clinical symptoms, the presence of the sacculations being discovered only upon postmortem examination. Sometimes, however, serious pathological processes ensue, as in Sydney Jones'[28] patient, who passed feces in the urine, in consequence of ulceration of the end of a diverticulum of the sigmoid flexure into the bladder. Alfred Loomis[29] found in the sigmoid flexure and colon descendens of a man 61 years old many highly inflamed diverticula filled with feces. Although no perforation had occurred, the inflamed diverticula had originated a general peritonitis. Two other cases of peritonitis, associated, however, with perforation, have been described by Fiedler. Klebs[30] has described a case of hernia obturatoria in which a diverticulum had perforated into the hernial sac. One of the favorable terminations of diverticula is, according to Fano,[31] obliteration through an increase in the connective-tissue elements. This is quite frequent in congenital but rare in acquired diverticula.

Case 1.—This is a museum specimen of a piece of jejunum 7½ cm. long, in the center of which is a small, oval diverticulum. No other diverticula were found in the intestinal tract. The peritoneum is smooth. The diverticulum is as large as a bean, and lies beneath the peritoneum of the mesentery at one side of the line of mesenteric attachment. Blood vessels run over its serous covering (Fig. 1). On the intestinal aspect the valvulæ conniventes are arranged in the normal way. An opening, which admits a small-sized probe, marks the point of communication between the intestinal canal and the diverticulum. This opening is very much smaller in size than the diameter of the saccule, and is surrounded by the valvulæ conniventes, three of which dip down into the

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mouth of the diverticulum, thereby almost closing the opening (Fig. 2).

Microscopic Examination: The diverticular walls are composed of mucosa, submucosa and serosa only. The muscularis stops abruptly at each side of the sac, where it is bunched as though the out-pouching mucous membrane had crowded it aside. The cells of the mucosa are very granular, and their nuclei stain but faintly. The lower portion of the mucosal hernia is highly inflamed. The submucosa is recognizable with difficulty. The muscularis shows faintly stained nuclei, but otherwise no change. The serosa is normal.

CASE 2.—Emma T., aged 59, a housewife, was admitted to the hospital suffering from pulmonary phthisis and interstitial nephritis. The autopsy, made by Dr. Hektoen, showed the body of a slender, emaciated woman. The anatomical diagnosis reads: False diverticula of the ileum, chronic pulmonary tuberculosis, chronic nephritis, chronic splenitis, atheroma of the aorta, atrophic liver, general marasmus.

The peritoneum was empty; the omentum adhered to the anterior abdominal wall. The mesentery was of full length. The lower part of the ileum was rather small in caliber; in the first meter and a half were numerous large and small, variously shaped diverticula. The large intestine was normal.

The diverticula are scattered along the mesenteric attachment of the ileum. They vary greatly in size, some being no larger than a split pea, while others are fully half the diameter of the intestine. The larger ones are often lobulated, so that a large diverticulum may present one or more smaller ones upon its surface. The sacculations are covered by peritoneum, which has often been loosened from its intestinal attachment by the out-pouching diverticulum. The larger diverticula show, for the most part, greatly constricted bases, while the smaller ones have broad and expanded ones. The diver-

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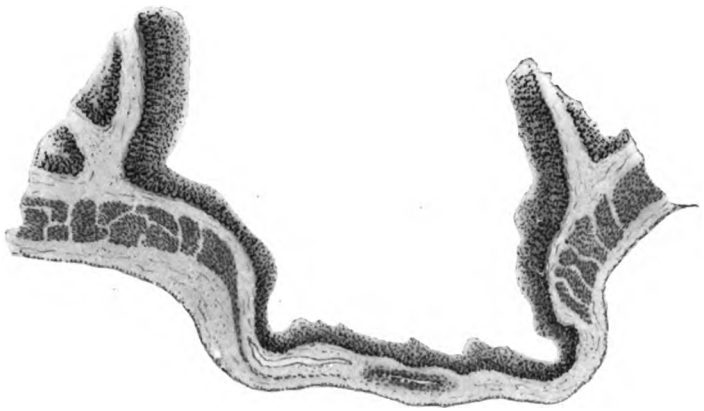

FIG. 4.

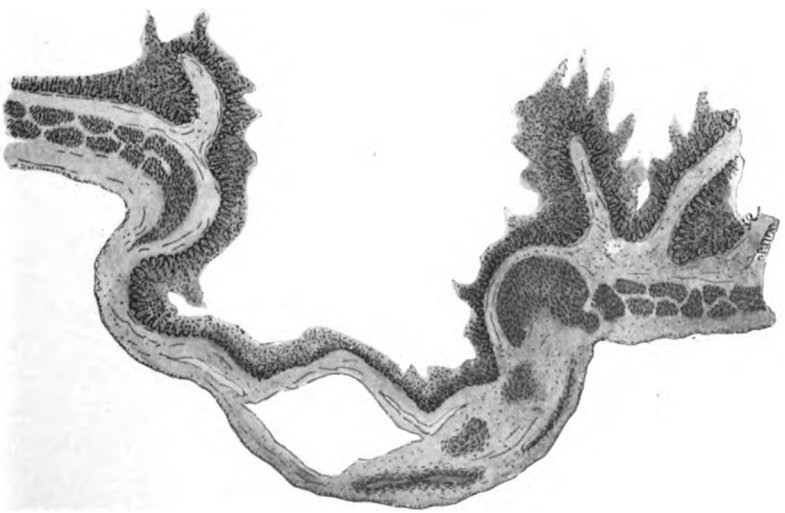

FIG. 5.

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ticula are not situated exactly between the two mesenteric layers, but usually show a greater bulging on one or the other side of the mesentery (Fig. 3).

There is an undoubted connection between the blood vessels and the diverticula. The larger diverticula have the blood vessels running over their surfaces; the smallest diverticula look as though blood vessels pierced their apices; at other times the blood vessels run over their surfaces.

Microscopic Examination: All of the diverticula are false, their walls being composed only of mucosa, submucosa and serosa. The muscularis is separated, the mucosa pushing through it to unite with the serosa and form the saccule (Figs. 4, 5 and 6). The mucosa of the diverticula is faintly stained, granular and atrophic. In the smaller diverticula it is markedly infiltrated with leucocytes. This inflammation is most marked at the apices of the mucosal hernias, and is most intense in the deeper parts of the mucous membrane. The muscular coat is lacking over the greater part of the diverticulum. On either side of the sac the musculature presents the normal appearance. In some of the specimens the muscular layer shows a sort of club-shaped thickening at the point where the diverticulum begins; sometimes a thin strip of muscular tissue is seen running a part of the way over the wall of the diverticulum at the sides (Figs. 4 and 5). When the latter occurs, the muscle thins out gradually until it finally loses itself in the subserous connective tissue. The serosa shows marked increase of connective tissue and often a small amount of round-cell infiltration. In the smaller diverticula a large blood vessel is usually found at the apex of the saccule. Sometimes more are found, depending in part upon the size of the diverticulum. All these vessels show much thickening of their walls. In no instance have I been able to find intestinal musculature about the blood vessels of the diverticula. Observations concerning the

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early development of the diverticula in this case are considered below.

CASE 3.—This specimen of false diverticula of the rectum, sigmoid flexure and descending colon, was kindly given me by Dr. Le Count.

William P., aged 64, laborer, was admitted to St. Elizabeth's Hospital complaining of pain across the stomach and in the right iliac fossa. The postmortem examination made by Dr. Le Count gave the following anatomical diagnosis: Diverticula of the rectum, sigmoid flexure and descending colon; hypertrophy of the heart; general arterio-sclerosis; chronic passive hyperemia of the liver, spleen, kidneys and lung; edema of the lower extremities; Meckel's diverticulum; right-sided obliterative pleuritis; slight chronic nephritis; edema of the brain.

There are adhesions about the splenic flexure of the colon and about the sigmoid flexure. The mucosa of the large intestine is everywhere smooth. In the rectum, sigmoid flexure and descending colon are found about twenty-five diverticula. The greater number of these are in the rectum and lower portion of the sigmoid. No diverticula are found above the descending colon. They are situated near the mesenteric attachment of the bowel and are from one-half to two centimeters in diameter externally. They differ somewhat in appearance, the smallest appearing as mere digital depressions in the mucosa. The diameter of the orifices is less than that of the saccules with which they communicate. In the larger diverticula labia of mucous membrane surround the openings. The walls of none have perforated, though some are extremely thin. An undoubted relation exists between the diverticula and the blood vessels. By holding the bowel to the light the vessels can be seen to enter the summit of the diverticula and then, branching, to run over their surfaces (Fig. 7).

Microscopic Examination: The diverticula are of

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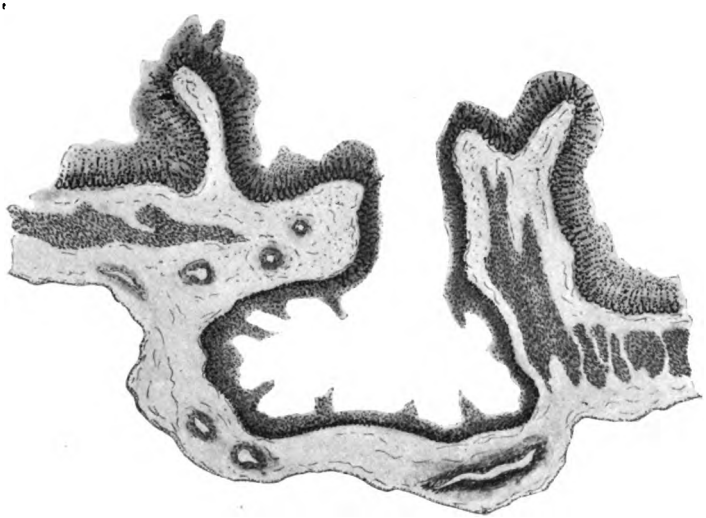

FIG. 6.

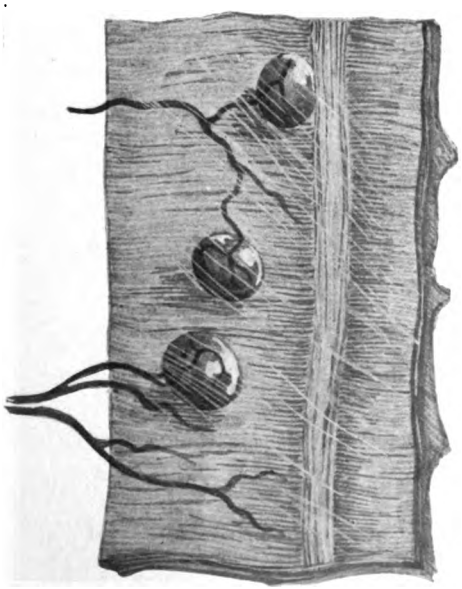

FIG. 7.

FIG 8.

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the false variety. The walls of the larger diverticula are composed of mucosa and serosa only, with intervening connective tissue, but the smaller, beginning diverticula show a muscular wall which has undergone thinning to a greater or less degree. The mucosa of the intestine in general shows no change, but the changes in the mucous membrane of the diverticula are in some places well marked. These consist of a granular disintegration of the cells associated with loss of nuclei, and an infiltration of the mucosa and submucosa in places with leucocytes. This evidence of inflammation is often most marked in the deeper portions of the diverticula, where, owing to the small diameter of the orifice, communication with the interior of the intestine is difficult. This case was found to be particularly suitable for the study of the early stages of development of diverticula and the results obtained are presented elsewhere.

CASE 4.—This example of diverticulum of the appendix was found in the dissecting-room of Rush Medical College. I have to thank Dr. Parker for bringing the case to my notice, and Mr. F. M. Wood for details of the pathological findings.

The specimen came from the body of a man about 50 years old, with pulmonary tuberculosis and general arterio-sclerosis. No history could be obtained. The vermiform appendix, bound down by firm adhesions, sprang from the lower and posterior part of the cecum, running inward, downward and backward so as to lie over the pelvic brim. It is 7½ cm. long and 7 mm. in diameter in its thickest part. It possesses a separate mesentery in which are found blood vessels and strands of connective tissue. Six centimeters above the tip of the appendix, on the side opposite the mesentery, is a sacculation measuring 12x11 mm., with a somewhat constricted base (Fig. 8). A few small blood vessels are seen running over its surface. A little below the site of the saccule, toward the distal extremity, a constriction

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extends half around the appendix, causing a diminution in its caliber. The appendix, with the diverticulum on the external aspect, is covered by shreds of torn fibrous adhesions. The mouth of the appendix is patulous. By probing, it is found that the lumen is patent only from the mouth to the constriction; beyond this point it is obliterated by connective tissue. The diverticulum and the patulous lumen of the appendix are filled with soft fecal matter in which are found several hard, irregularly shaped, calcareous granules, varying in size from grains of sand to fine gravel. The mucous lining of the patulous lumen is smooth; the wall of the appendix is thickened. The wall of the diverticulum is no thicker than tissue paper; its lining is slightly roughened.

Microscopic Examination: The obliterated part of the appendix shows the lumen to be entirely filled up by a loose network of connective tissue; no evidences of mucosa are visible. External to the loose connective tissue is a ring of dense mature connective tissue entirely encircling the appendix. This is evidently the much thickened submucosa. The connective tissue in both these places shows many newly-formed blood vessels, The muscularis consists of a thick internal circular and a thick external longitudinal coat. No degenerative changes are visible in either layer. The serosa is thickened and presents, at the points corresponding to the torn adhesions, a ragged peritoneal edge. None of the normal lymph follicles are present, and no evidences of an acute inflammatory condition can be found. At the constriction below the diverticulum there is entire loss of the muscular coat, the wall of the appendix here being made up of the connective tissue of the submucosa and the slightly thickened serosa (Fig. 9). The mucosa over the constriction and extending above and below it, is highly atrophic, remnants only of the crypts being left; at the site of the constriction the mucosa is covered by a thin layer of deeply stained, granular detritus. The

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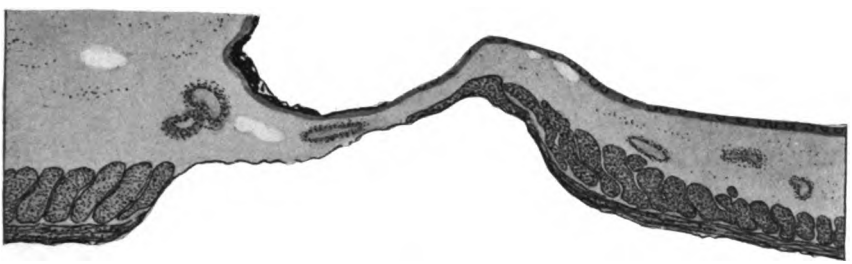

FIG. 9.

FIG. 10.

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submucous connective tissue is greatly thickened and here and there are many well-filled, newly-formed blood vessels; many large empty spaces are present between the strands of connective tissue. No lymph follicles are seen. The muscularis stops abruptly at the lower side of the constriction and more gradually at its upper; the internal layer is thick, the external somewhat thinned. The connective tissue of the serosa is slightly thickened.

The mucosa opposite the large diverticulum is represented by the remains of a few crypts The enormously thickened submucosa here constitutes the greater part of the wall. It is not inflamed, but many well-filled blood vessels are seen. Both muscular layers are much thinner than in the sections already described. The serosa is somewhat thickened, so much so at one point that a wedge-like mass of connective tissue has taken the place of the outer muscular coat. The fibrous tissue shows outward pouching.

The wall of the diverticulum is everywhere extremely thin (Fig. 10). The mucosa of the appendix becomes gradually lost as it merges into the diverticular lining, which is represented by a deeply stained blue line of fecal matter, no actual mucosa being visible. The wall is composed only of submucosa and serosa. The muscularis is gradually lost at the point where the diverticulum begins (Fig. 10). Many large blood vessels are found in the wall of the diverticulum. The peritoneal surface shows many torn strands of connective tissue, but no changes of an acute inflammatory nature are seen.

* * *

Case 1, in being an example of a single diverticulum of the jejunum, contrasts with the cases of jejunal diverticula reported by Virchow,[21] Edel,[5] and Nicholls,[32] which were all of multiple diverticula, such multiplicity being the rule with this type of diverticulum. Roth[17] and others have recorded instances of a single diverticu-

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lum of the duodenum, and Bristowe[19] one of a solitary diverticulum of the ileum. The gross and microscopic appearances of the diverticulum in Case 1 were those characteristic of false diverticula. The intimate relation to the blood vessels is to be emphasized. The marked inflammation of the mucous lining of the sac is an interesting feature.

Case 2 is similar to those already cited from Wallmann, Birch-Hirschfeld, Hansemann and Klebs. Hansemann has called attention to the fact that the diverticula in his case did not go directly into the mesentery, but lay to one side of it. This same condition has prevailed in both my cases. The tunicary hernia of the jejunum, though covered on all sides by peritoneum, still lay entirely on one side of the mesentery; likewise in the diverticula of the ileum, though some lay just between the mesenteric leaves, the majority showed most prominently on one side of the line of attachment of the mesentery.

My case of diverticula of the ileum is interesting inasmuch as it shows clearly the intimate connection between the blood vessels and the sacculations. A systematic study of the variously sized diverticula has shown the following points:

The smallest diverticula which could be found—diverticula macroscopically about the size of a split pea—show within the serosa a blood vessel with much thickened walls. On either side of this vessel may be seen a beginning down-dropping and protrusion of the mucosa. This gives the mucosa a W-shaped appearance, with the blood vessel contained between the two middle arms (Fig. 4). Diverticula somewhat larger show a greater protrusion of the mucosa and an outward movement of the blood vessel at the apex of the saccule (Fig. 5). Thus the blood vessel is borne outward by the out-pouching diverticulum. At this stage of development, it seems that one side of the saccule may grow faster than the other,

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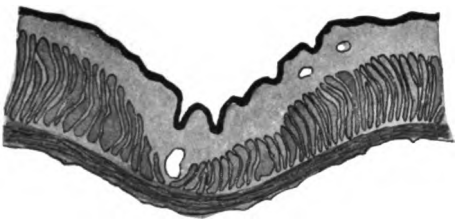

FIG. 11.

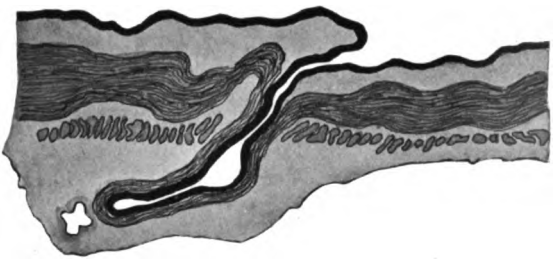

FIG. 14.

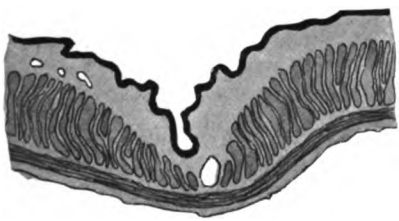

FIG. 12.

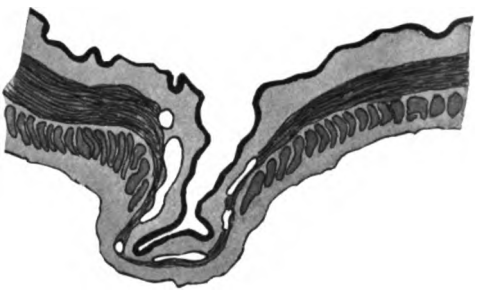

FIG. 15.

FIG. 13.

FIG. 16.

FIG. 17.

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so that ultimately the blood vessel is seen to lie at one side of the diverticulum (Fig. 6).

This matter of development indicates that the location of a large blood vessel in a certain place in the muscularis of the intestine produces here a locus minoris resistentiæ; a causative agency of some kind produces an internal pressure which manifests itself by a hernia of the mucosa at the point of least resistance; as no muscular tissue of the intestine is ever found to surround the blood vessel of the diverticulum, it seems reasonable to suppose that the false diverticulum is formed by a protrusion of the mucosa along the sheaths of the blood vessels.

Conditions favorable to diverticular formation were present in this case. There was a general marantic condition with chronic pulmonary tuberculosis and chronic nephritis; the intestine, through its entire extent, was thin and flabby; the lower part of the ileum was of small caliber, a condition which, if not due solely to agonal contraction, might at least favor the production of diverticula in the upper part. The inflammatory condition of the mucosa and serosa is also worthy of note.

The detailed study of the process of mucosal hernia through the muscular coat is not so simple as might at first seem to be the case. In the two cases of diverticula of the small intestine above described the thinness of the muscular coat prevented a careful study of the part played by each of the layers, but the thickness of the muscular sheath of the sigmoid and rectum permitted me to study in Case 3 to better advantage the participation of each in the production of the diverticulum.

As the studies of Hansemann[4] and Graser[35] have shown, the veins draining the intestine pierce the inner muscular layer, run between the two muscular layers, and finally pierce the outer longitudinal layer to make their appearance externally. Graser finds, as previously Hansemann had done, that false diverticula follow the

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venous sheaths. His view concerning their formation in the sigmoid flexure, to which his studies were limited, is briefly this: A congestion of the veins of the sigmoid brings about dilatation of these vessels, causing thereby a locus minoris resistentiæ in the muscular tunic of the intestine; an intra-intestinal pressure such as the presence of gas or feces furnishes the initiative force required to produce the diverticula at these points of least resistance.

My case (Case 3) of diverticula of the rectum and sigmoid flexure corroborates to a great extent the views advanced by Graser. The blood vessels throughout the specimens examined showed marked congestion, being very large and filled with blood, and there was little difficulty in tracing the connection between the diverticula and the distended blood vessels. The smallest diverticulum that I was able to find—one that showed macroscopically as a slight digital depression in the mucous membrane—showed the beginning stages of the mucosal hernia. Corresponding to the slight invagination of the mucosa, within the inner layer of the muscular tunic was found a large congested blood vessel; on either side of this a well-marked thinning of the muscular sheath had already occurred; this thinning was most evident in the inner muscular layer, the outer layer being still intact (Fig. 11). A somewhat larger diverticulum showed on histological examination a greater depression of the mucosa with a greater thinning of the inner muscular layer (Fig. 12). For some time at least, the outer longitudinal muscular layer may remain intact, being pushed more and more outward by the protruding mucosa (Fig. 13). As the diverticulum continues to grow the muscular layer surrounding it becomes very much thinned and finally disappears entirely, so that the wall of the diverticulum is ultimately composed of mucosa, submucosa and serosa only.

The foregoing description does not, however, apply to

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all the diverticula. Although the inner, circular coat usually seems to be the one to give way first, it sometimes happens that the outer shows the first break in its continuity. It would seem that in these cases the blood vessel had occupied the outer layer of the muscular tunic, in this way changing the locus minoris resistentiæ from the inner to the outer layer of the muscularis. Thus such conditions as I have pictured in Fig. 14 come to pass, in which the mucosa and the inner muscular layer rupture through the outer one. In this process the blood vessel is evidently pushed ahead of the oncoming diverticulum.

Finally, it would seem that under some conditions a break occurs simultaneously in both layers of the muscular sheath. This occurs in those places where several large vessels are situated closely together, so that the entire muscular wall is so weakened that the mucous membrane breaks through both with comparative ease (Fig. 15).

It is now the generally accepted belief that the diverticula follow the paths of the venous sheaths (Figs. 16-17); still, though this be in the main correct, I can not accept it in its entirety. Although the presence of the blood vessel is the prime, predisposing cause leading to the production of the mucosal hernia, still, once started, the saccule follows the path of least resistance. This may or may not be the sheath of the blood vessel. Instead of following the latter, the mucous membrane may spread between the layers of the muscular tunic (Fig. 13), or it may spread through the connective tissue between the muscularis and the serosa in places where it is impossible to establish any connection between the diverticulum and the blood vessels.

The partially successful effort of nature to limit the enlargement of the diverticula is evidenced by the connective-tissue hyperplasia about them. The thickness of the serosa covering the diverticula is usually almost directly proportional to their size; and there can be no

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doubt that to this protective attempt of nature is due the infrequency of perforation of diverticula into the peritoneal cavity.

Doubtless an important factor in the causation of the diverticula in Case 3 was the chronic passive congestion of the viscera due to hypertrophy and dilatation of the heart and arterio-sclerosis. While this factor has not the exclusive importance attached to it by Graser, it is certainly one of the demonstrable predisposing causes of intestinal diverticula. Constipation furnished another condition favorable to the process by increasing the intra-intestinal pressure.

The presence in this case of firm adhesions about the rectum and sigmoid, corresponding to the position of the diverticula, is also of interest. As has been stated, some of the diverticula were highly inflamed. It can readily be understood how easily these pockets, communicating as they do through only small openings with the lumen of the intestine, might harbor fecal matter, the accumulation of which might lead to an inflammatory condition. How difficult the removal of such material may be is evident from Fig. 13, which shows a section through one of these highly inflamed diverticula. Graser has pointed out the relation which may exist between diverticula of the lower bowel and chronic pelvic peritonitis. I interpret the adhesions which were formed about the sigmoid flexure in my case as an evidence of such a chronic pelvic peritonitis engendered by the inflammatory condition of the diverticula. Further evidence of such a peritonitis is found in the pain in the iliac fossa of which the patient complained. A few diverticula were found in the region of the beginning descending colon, and here, too, slight adhesions had formed.

Case 4 is an example of diverticulum of the vermiform appendix—a condition concerning which but little has been written. Finkelstein[36] has suggested the possibility of the production of a diverticulum from increased

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intra-appendicular pressure following occlusion of the mouth of the appendix and consequent collection of secretion. Two cases have been recorded. That of Kelynack[26] was of an appendix which became cystic in consequence of obstruction to its opening. Two very distinct diverticula communicating with the lumen of the appendix were found between the folds of its mesentery. No muscular tissue was detected in the walls of the diverticula and hence the conclusion seems justifiable that they were mucosal hernias through the muscularis in consequence of the pressure produced by the stasis of the secretions within the appendix.

In Ribbert's[27] case there was a group of small cysts of varying size, arranged in a grape-like cluster at the mesenteric border of an apple-sized cyst of the appendix and communicating with the latter through larger and smaller openings. The large cyst was the result of occlusion of the mouth of the appendix. The small cysts are interpreted by Ribbert as dilated glandular cysts which had become partly occluded and separated from the mucosa. If this interpretation be correct, these cysts would not be analogous to the ordinary false diverticula of the intestine.

In some respects, more like my case is the one reported by Edel,[5] who found in a man 69 years of age a pea-sized false diverticulum, situated on the side opposite the mesentery, 2 cm. from the distal end of the appendix, which was 8 cm. in length. A small blood vessel ran over its surface. There were no fecal contents in the appendix or diverticulum, and its lumen was patent. The muscularis was absent over the diverticulum. The mucous membrane was atrophic; the serosa showed many new blood vessels. By the side of the diverticulum the muscle was replaced by a wedge-shaped mass of connective tissue, which, though of unknown origin, was thought to represent a scar. For the formation of the diverticulum in this case Edel offers the following explanation: The

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scar produced a slight traction upon the mucosa and, as the result of connective-tissue increase in the serosa, the latter began to bulge out. Assuming that the traction upon the mucosa increased, and that the muscularis finally yielded to the slight but continued pressure of the mucosa, he was led to believe that the production of a false diverticulum thereby resulted.

I am unable to say what caused in my case the mass of adhesions found about the appendix and its diverticulum. A tuberculous or syphilitic etiology is possible. There were no acute inflammatory lesions, and in the absence of a history we must leave this point unexplained. If we believe with Ribbert that obliteration of the appendix represents a process of involution and not one of pathological change, then little is to be said concerning the obliteration of the lower part of the appendix in my case. Loss of lymph follicles and replacement with hyperplastic connective tissue are both found, so that all the conditions described by Ribbert as characteristic of this type of obliteration are represented.

The constriction of the appendix on the distal side of the diverticulum is interesting in so far as it presents the typical structure of a false diverticulum without a bulging of the weakened part. The wall of the appendix at the point of the constriction is covered with a mucosa upon which lies a deeply-stained granular detritus. Longitudinal serial sections passing from the non-constricted into the constricted portion of the appendicular wall show a progressive thinning of the muscular coat, ending finally in its total loss (Fig. 9). Under ordinary conditions, we would expect the mucosa to bulge outward as the muscular coat became thinner, still in this case, the opposite has occurred and the serosa has fallen in toward the mucosa. This seems to me to be a natural sequence when we remember that the connective tissue of the submucosa is fully four times as thick as, and hence, firmer and more unyielding than the connective

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tissue of the serosa. Thus, instead of the formation of a diverticulum, a constriction has resulted.

The cause of the production of the large diverticulum can at best only be surmised. As in Edel's case, it occurred on the side opposite the mesentery, so that its formation as a mucosal hernia along a vascular sheath is extremely unlikely. It may be recalled that the appendix was embedded in firm adhesions; that the diverticulum was filled with fecal matter; and that the wall was composed of thickened serosa only. True intestinal diverticula due to traction produced by an accessory pancreas, or by connective-tissue bands in the mesentery have several times been described. It seems to me not impossible that in the beginning this diverticulum of the appendix was a true one, due to the traction of a connective-tissue band, and that this mural bulging became filled with fecal matter, the accumulation and stagnation of which caused a pressure atrophy of the mucosa and muscularis of the diverticulum. Thus the wall of the diverticulum became weakened and composed of connective tissue only.

As we have no means of learning whether the adhesions antedated the diverticulum, another explanation may also be suggested. It may be that in consequence of the pressure and irritation of feces accumulated in the appendix the mucosa first and then the muscularis underwent necrosis or simple atrophy. There would thus be produced in the wall of the appendix that which is essential to the formation of a diverticulum in any part of the intestinal tract, namely, a point of lessened resistance, which, under the further influence of an increased intra-intestinal pressure, as from meteorism or constipation, might readily be the starting point of a diverticulum presenting the histological features observed.

The possibility may also be considered that the same process, whether pathological or referable to simple involution, which had caused the constriction, may have affected a limited area in the wall of the appendix caus-

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ing a focus of lessened resistance, which yielded to the normal or perhaps increased pressure within the lumen of the appendix, before any considerable compensatory new connective tissue had formed

I am indebted to Professor Hektoen for much kind assistance in this investigation and in the preparation of this paper.

November 13, 1899.

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DESCRIPTION OF PLATES.

Fig. 1.—Case 1. Jejunum, showing the relation between the blood-vessels and diverticulum.

Fig. 2.—Case 1. Arrangement of the valvulæ conniventes of the jejunum about the diverticulum.

Fig. 3.—Case 2. Ileum, showing the intimate connection between the diverticula and the blood-vessels.

Fig. 4.—Case 2. Section of a diverticulum in process of formation. The atrophic mucosa is seen dipping down on either side of the blood-vessels. The muscularis is much thinned on the left and entirely absent on the right side of the diverticulum.

Fig. 5.—Case 2. A later stage of development of a diverticulum. The muscularis is missing in the wall of the diverticulum. On the right it has been crowded aside by the out-pouching mucosa. Several blood-vessels with much thickened walls are seen in the wall of the diverticulum on the right.

Fig. 6.—Case 2. Section of a mature diverticulum with greatly thickened subserosa. The left side of the diverticulum has evidently grown more rapidly than the right. A large blood-vessel is seen in the right wall of the diverticulum. The mucosa has undergone marked degeneration.

Fig. 7.—Case 3. False diverticula of the sigmoid flexure. The blood-vessels are seen running over the surfaces of the diverticula.

Fig. 8.—Case 4. Appendix vermiformis, showing diverticulum, constriction and mesentery. The adhesions are not shown.

Fig. 9.—Case 4. Section through constriction of appendix. The muscularis is wanting in this portion of the wall of the appendix.

Fig. 10.—Case 4. Section through diverticulum. The subserosa and the submucosa of the appendix are seen to merge into a single layer to make the wall of the diverticulum.

Fig. 11.—Case 3. First stage in the formation of a diverticulum. The mucosa is dipping downward toward the dilated blood-vessel in the somewhat thinned internal coat of the muscularis.

Fig. 12.—Case 3. A later stage of the same. The muscularis has become still thinner about the blood-vessel.

Fig. 13.—Case 3. The mucosa has broken through the internal coat of the muscularis and has pushed the external coat ahead of it. A lateral pouching of the mucosa has taken place between the internal and external layers of the muscular tunic. The subserosa is much thickened, and in it are several blood-vessels.

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Fig. 14.—Case 3. The mucosa in this instance has pushed the internal muscular coat ahead of it, and with it has broken through the external one. A large blood-vessel is seen at the apex of the diverticulum.

Fig. 15.—Case 3. Simultaneous rupture of both muscular coats of the intestine. Attention is called to the great number of large blood-vessels found in and about the muscularis at the site of rupture.

Fig. 16.—Case 3. A diverticulum in close relation with a blood-vessel.

Fig. 17.—Case 3. A diverticulum, associated with rupture of both muscular coats of the intestine, making its way along the sheath of a blood-vessel.

Addendum.—Since the completion of this paper I have examined two additional cases of false diverticula of the sigmoid and rectum (in one case with also a few diverticula in the descending colon) both being in tuberculous men—40 and 60 years old—with chronic passive congestion from cardiac and vascular disease. There were 25 diverticula in one, and 10 in the other case. The histological conditions were like those in Case 3.

A PECULIAR GASTROLITH LEADING TO PERFORATION AND DEATH.

MAXIMILIAN HERZOG.

The author presented a gastrolith and said that the undigestible foreign bodies found in the human stomach might be classified into a number of groups, such as foreign bodies found in insane individuals, who, as is well known, often swallow the most heterogeneous articles, so that they sometimes give rise to stories of "human ostriches." Foreign bodies swallowed accidentally by sane people, particularly sets of teeth, or swallowed in small instalments, such as bit off hairs (hairballs). Further,

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foreign bodies in the nature of resinous substances (shellac) formed as precipitates from alcoholic solutions. A number of cases of the latter type have been reported in Germany. Such resinous gastroliths occurred in laborers addicted to alcohol and working with alcoholic solutions of shellac, of which they freely partook. The alcohol is absorbed, but some of the shellac always remains behind. In one instance a shellac stone weighing near to a pound and a half was found. Lastly, there are the foreign bodies found in the stomach of children.

The case presented belonged to the latter class; it occurred in the practice of Dr. Charles H. Cargile of Bentonville, Ark., who furnished the following data: The mass was removed postmortem from a male child 3 years old. The boy, while being left alone in a garden, ate very freely of persimmons and in one or two hours afterwards vomited much; the vomitus consisting mostly of pulp, peel and seeds of this fruit. Excepting slight vomiting daily and the very easy palpation of the mass in the epigastrium, there was nothing abnormal in the condition of the child until sudden and violent symptoms of perforative peritonitis occurred, about ten weeks after the repast. Death ensued 18 hours after the symptoms of peritonitis presented themselves. Autopsy revealed peritonitis. The abdomen contained more than a pint of semi-opaque fluid. Before opening the stomach there was found a perforation on its anterior wall near the greater curvature. Corresponding with this, and beneath was the somewhat sharp edge of a persimmon seed that projected above the surface of the concretion and doubtless caused the perforation. The stomach was dilated. When fresh, the gastrolith was 5¾ inches long, 1¼ in diameter at its pyloric end and 1¾ at its greater curvature. The gastrolith presented a complete cast of the stomach. In its fresh state this was still better shown than now, drying and great shrinkage having changed its shape to some extent. This

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shrinkage has not been alike in all parts on account of the unequal distribution of its component parts and their unequal tendency to dry and shrink. This is especially noticeable in the lesser prominence of the seed that caused the perforation. When shaken the seeds within rattle. When the gastrolith was fresh and moist, a substance that looked like starchy matter, constituted quite a part of it. It was enveloped in a coating from one-fourth to one-half inch thick, of a doughy substance, small parts of which had escaped through the perforation and constituted the flocculent bodies floating in the serous fluid in the abdomen.

For the information of those in sections where persimmons are not found, it is proper to state that they are larger than plums, with seeds flatter and a little larger than those of prunes, and each persimmon contains about one-half dozen seeds. More than a dozen of these seeds can be seen on the surface of the mass described.

In the dried condition the gastrolith now weighs 46 grams; it still forms a pretty good cast of a human stomach. Its longest diameter is 11 cm.; the other dimensions are 4x5 cm. A chemical examination has not yet been made, but it appears that most of the mass is cellulose.

May 13, 1901.

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REPORT OF A CASE OF DIFFUSE INFILTRATING SARCOMA OF THE LIVER WITH WIDELY SCATTERED METASTATIC TUMORS SECONDARY TO A SARCOMA OF THE EYE.

E. R. LE COUNT.

Abstract of the Clinical History.

The patient, a man about 50 years of age, was referred by his family to an oculist three years ago; the oculist found a dislocation of the retina and later diagnosed a tumor of the fundus, and advised the removal of the eye. The operation was refused. The patient's health remained good until about six months ago, when he noticed that he was losing in strength, and he experienced at this time some distress in his stomach. Ten weeks before death he came under the care of Dr. J. B. Herrick, complaining of poor appetite. At this time examination showed: Emaciation and cachexia, general weakness, slight enlargement of the liver and just below the costal arch two subcutaneous nodules, one of which was slightly pigmented. There was also found an enlarged lymph gland at the right angle of the jaw and the right eye was blind. A dark mass could be seen through the pupil, and its black color showed through the sclera. The subsequent history was, briefly: Increase in cachexia, rapid enlargement of the liver, the development of ascites and many subcutaneous nodules, severe attacks of dyspnea and the accumulation of fluid in the right thoracic cavity. The necropsy was done seven and one-fourth hours after death.

ANATOMIC DIAGNOSIS.

1. Metastatic sarcomata of the lungs, heart (pericardium), pancreas, liver, thyroid, cervical, mediastinal and retroperitoneal lymphatic glands, of the mesentery and

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of the mucous coats of the esophagus, stomach, gall-bladder and intestines.

2. Hydrothorax (right side).

3. Adhesive pleuritis.

4. Compression atelectasis of the middle and lower right lobes.

5. Chronic nephritis.

6. Nephrolithiasis.

7. Chylous retention cysts of the small intestines.

8. Mural thrombi of the heart and pulmonary veins.

9. Fibrous myocarditis.

NECROPSY.

External Examination.—The height of the body is 186 cm. It is of a large frame, somewhat emaciated and very anemic. Rigor mortis is marked, as is also the posterior lividity; it is a mottling instead of the usual diffuse reddening. There are numerous subcutaneous nodules located beneath the skin on the anterior surface of the body. They feel like shot and beans just beneath the skin, and some are bluish. They are more numerous and larger on the right side of the body. The pupil of the right eye is widely dilated. The abdomen is distended and the walls tense; distension is more marked on the right side.

Internal Examination.—The subcutaneous adipose tissue exposed by the median incision is scanty in amount. The liver extends downward below the navel, so that its lowest level is three fingers' breadth below the highest point of the crest of the ilium. The notch of the transverse fissure of the liver in front is to the left of the median line. There is a large amount of clear fluid in the abdominal cavity. The diaphragm extends upward to the lower border of the fifth rib on both sides. There are no adhesions about the spleen or gall-bladder. The appendix lies coiled up behind the cecum in the right iliac fossa. The peritoneum is smooth and glistening everywhere. On opening the cavity of the lesser omen-

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tum there are seen two large fungous tumor masses which project forward into its cavity. They are in the mesentery of the transverse colon and lie saddle-like across the vertebral column. The larger of these lies on the left side; it is the size of a small fist and quite dark colored. The smaller one to the right of the vertebræ is the size of a hen's egg and very nodular; it is separated from the stomach with great difficulty. In the mesentery of the sigmoid are numerous small dark tumor masses; the largest of these is the size of a hickory nut; nodular externally and pigmented in spots. On opening the thoracic cavity a large amount of clear slightly blood-stained fluid escapes (approximately 2250 c .c). The right pleural cavity is free from adhesions; in the left pleural cavity the lung is bound to the chest wall by quite easily broken adhesions; this cavity contains a small amount of fluid. The pericardial cavity contains some clear fluid (approximately 200 c. c.). Its layers are smooth.

Heart.—The apex is rounded; there is a large amount of fat externally, especially over the right ventricle. On the middle of the right ventricle is a small pigmented nodule in the fat, measuring 3 mm. in diameter. The heart measures externally 13 cm. long, 13 cm. broad at the broadest point, 7.5 cm. thick; its weight unopened is 465 gms. There is a distinct hemorrhage in the subpericardial fat in front, opposite the interventricular septum; it measures 6 mm. in diameter. There are some minute ecchymoses at the base of the heart in the pericardium about the origin of the great vessels. On the posterior surface of the right auricle is a delicate, somewhat granular, easily removable, fibrinous exudate. The aortic and pulmonary valves are competent to the water test. There is partially clotted blood in both ventricles and in the right auricle; these clots weigh 29 grams. The mitral valve admits three finger tips readily; the tricuspid five.

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In the lower part of the right auricular appendage are some ivory-colored, rounded, adherent, firm bodies. These are very minute, but located at many separate points between the muscular trabeculæ of the wall. There are also some in the trabeculæ of the right ventricle at the apex of the heart; these are larger, some as large as peas; they are also adherent, firm, smooth externally, and ivory white. There are several aberrant chordæ tendineæ in the right ventricle. There are no changes about any of the large valves of the heart, except the tricuspid, which is thickened at its free margins. The endocardium is smooth and the foramen ovale is closed. The left ventricle is 8.5 cm. long; its wall is 13 to 17 mm. thick. The right ventricle is 9 cm. long; its wall is unusually thick—from 4 to 6 mm. The myocardium is somewhat mottled, rather soft, and on section there are masses of fibrous tissue seen around the small blood vessels.

Lungs.—The right lung weighs 435 grams. The upper half of the upper lobe is spongy and inelastic. On its posterior surface is a small sessile growth on the pleura; a similar larger growth is found close by; both are whitish and firm; the larger measures 3 mm. in diameter. The pleura is marked by dark lines of coal pigment; it is smooth. At the apex the pleura is thickened and firm; there are no changes in the underlying lung parenchyma. The upper lobe floats; it contains no consolidated portions. The two lower lobes sink in water when cut free from the lobe above; they are absolutely noncrepitant. The middle lobe is much smaller than normal. On its surface are several sessile and pedunculated yellowish-white growths. There is an area of consolidation in this lobe just beneath its posterior surface which measures 1 cm. in its longest dimension. It is wedgeshaped, very firm, and filled with dark blood. Near the root of this lobe is a tumor mass measuring 13 mm. in its longest dimension. On section it is rather white

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and firm throughout. The lower lobe is very dark externally and soggy; it is much smaller than normal. Externally there are a few small nodules similar to those seen on the upper lobes; the largest measure 4 mm. in their longest diameter. In the substance of this lobe are some larger nodules (2 or 3) yellowish-white on section and quite firm. The bronchial glands at the root of the right lung are slightly enlarged and deeply pigmented.

The left lung weighs 660 grams. The interlobular fissure is quite obliterated by firm adhesions. It floats and crepitates throughout. There are firm masses of fibrous tissue on the upper lobe near the fissure; they form a zone which borders the fissure above. In places the two pleural sheets have adhered and are present on the lung. At the apex is a pleural scar similar to that seen on the right lung; the lung tissue beneath is unchanged. The anterior margin of this lobe is very emphysematous; on section this lobe contains a large amount of frothy serum. The lower lobe is quite smooth externally; it shows but few changes. There are no tumor nodules on the surface of the left lung; at its root are white clots occupying the large blood vessels; they are adherent to the vessel wall in places.

The tongue and tonsils were not removed; the esophageal lining shows signs of postmortem digestion for its entire length. Near the lower end of this canal is a firm white nodule 2 mm. in diameter, located beneath its mucous lining. The cervical glands are enlarged on the right side of the neck, but on section they are mottled with firm white and bluish areas. The epiglottis and vocal cords show no changes. The tracheal mucous lining is covered with a brownish mucus; when this is removed the surface is white and smooth. From the loose mediastinal tissues about the trachea and at its bifurcation 35 to 40 small nodular tumor growths were easily dissected. They are about the size of peas, firm, gener-

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ally yellowish-white, although some are pigmented. Some are as large as 1 to 2 cm. in diameter.

The *thyroid gland* weighs 75 grams. Its right lobe is much larger than the left; the former measures 7.5x5.5x 3.5 cm.; it extends upward to a level just below the upper border of the thyroid cartilage. This lobe is very firm; on section through its longest diameter the lower three-fourths is found occupied by a mottled tissue which resembles granite in color; many nodules have fused to produce this appearance and some of these are pigmented. The left lobe measures 5.5x3.5xl cm.; it weighs 16 grams. On section there are some whitish discrete nodules of new tissue, located for the greater part in the posterior part of the lobe; the largest measures 4 to 5 mm. across.

The *spleen* weighs 147 grams and measures 12x8x3.5 cm. It is very smooth externally and of a dark red color; the cut surface is dark colored; its substance is soft; the Malpighian bodies are plainly visible and there are no masses of tumor tissue found in many sections of it.

The *liver* weighs 5360 grams and measures 33x30x14.5 x6 cm. The chief increase in size is in the right lobe, which is enlarged both downward and from before backward. A large part of the anterior surface of the right lobe, the under surface of the right lobe and the surface of the quadrate lobe are all mottled and roughened by minute pale raised areas; these have produced a profuse light colored raised surface which extends over the most of the upper lobe. Between this raised surface and the unchanged liver tissue to the left is a dusky red zone. The left lobe and a small part of the right lobe near it show no changes. On section the right lobe is seen to be occupied for its greater part by new tissue made up of minute yellowish-white nodules which have coalesced; very few show any signs of pigmentation. The liver tissue around is hyperemic like a nutmeg liver. There are no changes in the left lobe.

The common bile duct is open; the gall-bladder is par-

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tially filled with a viscid brown bile that contains stringy mucus. On the lining of the gall-bladder are two small nodules the size of birdshot; they project somewhat and one of them has a very dark summit.

The *stomach* weighs 225 grams. It measures in its longest transverse diameter 27 cm., in its longest vertical diameter 12 cm. There are six small nodules on its inner surface; they measure 2 to 5 mm. in diameter and are quite firm; two are slightly pigmented. On the outer surface of the stomach, hanging from delicate tags of fibrous tissue, are several firm disk-shaped nodules. The largest is the size of a silver quarter; they fringe the lesser curvature. The pyloric orifice admits one finger tip easily; the inner surface of the stomach is gray and clean.

The *pancreas* weighs 140 grams. It measures 21 cm. long, 4.5 cm. in width, and 1.5 cm. in thickness. A large tumor mass in the mesentery of the transverse colon has invaded the tail of this organ and produced there, a softened dirty black tissue. There are found on section small islands of pale tumor tissue entirely within the pancreas; these are not numerous, but are quite widely distributed. The intervening pancreatic tissue shows no changes.

Intestines.—The walls of the duodenum are thickened; Brunner's glands give to its lining a granular appearance. In the tissue around the duodenum are numerous small tumor nodules. The mucosa of the jejunum is rather pale; it is quite clean. At slight intervals in the mucous membrane and freely movable with it are small elevations of a chalky white color; they are frequently located on the valvulæ conniventes; on slight pressure or on section they exude a milky fluid. About one centimeter below the pyloric orifice is a large spherical mass of new tissue projecting from the lining of the intestine; it is 1 cm. in diameter and projects 4 or 5 mm. and has a flattened grayish-brown summit. There are some smaller similar nodules which are pigmented and

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projecting, located at intervals throughout the small intestine. Peyer's patches are flat, smooth and pale. The lower end of the ileum is very thin. Tumor nodules are more scarce in the lower half of the small intestine than in the upper half. The appendix measures 7 cm.; it is thick and contains a fecal concretion the size of a pea. In the upper part of the cecum a tumor nodule the size of a buckshot is located opposite the mesentery in the submucous coat. The lining of the colon is quite clean. Some smaller nodules are present in the colon in its transverse and descending portions; some are just beneath the serous coat, and some just beneath the mucous coat. Where the sigmoid and rectum join, a tumor nodule 2 cm. in diameter forms a polyp-like growth on the outside of the canal where the appendages (epiploicæ) hang.

In the fat about the kidney can be felt apparently hundreds of small and larger tumor nodules. From that about the right kidney thirty were easily dissected which averaged 4 to 5 mm. in diameter. From the perinephritic fat of the left kidney and region about the aorta, sixty such nodules were easily obtained.

The left *kidney* weighs 179 grams. It is 12x5.5x4 cm. in size. The capsule is adherent in places and the underlying surface is granular. There are some areas which project externally; one of these on the posterior surface of the kidney has a dark center and a light colored margin; it measures 13 mm. in diameter; on section a clear fluid escapes, and its walls are firm and smooth and made up of compressed kidney tissue. At the lower end of this kidney in one of the calices are some brownish-yellow finely granular calculi. The mucous membrane of that calyx is reddened by minute engorged blood vessels. In one of the pyramids is a small, firm, whitish body the size of the head of a pin. On the outside of the kidney is a small yellowish area near the hilus, which is softened; it measures 1 mm. in diameter; also, a larger

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tumor nodule which measures 1 cm. in diameter; this is adherent to the kidney, but located mainly in the capsule and perinephritic fat. There are no very large tumor masses found in the substance of this kidney. The cortical markings are distinct, glomeruli are prominent and red.

The right *kidney* weighs 190 grams. It measures 12.5 x6x3 cm. On its posterior surface and at the upper end is a large nodule 2.5 cm. in diameter which projects from the surrounding surface 1 cm. It is yellowish-white in its center, and the margin is livid when viewed externally from the presence of minute vessels. At the opposite end of the kidney is a large cyst, which ruptured in removing the capsule, and a clear brownish fluid escaped. In the calices about this cyst are many minute calculi similar to those seen in the left kidney. A tumor nodule is seen, on sectioning the kidney, located at the base of a pyramid, measuring 2 mm. in diameter. The large nodule seen externally when sectioned is found to be made up of soft tissue which is bloody; the surrounding kidney tissue is white and compressed to such a point that it resembles a capsule for the tumor mass.

The left *adrenal* weighs 13 grams. It is 6.5 cm. long, of normal shape, and when cut the medullary region appears abnormally wide, white and firm. The right adrenal weighs 11 grams. It is thin and shows no changes when sectioned. There are small tumor masses about it In the *mesentery* of the small intestine there are numerous nodular tumor masses. Many of these project from its upper surface. As a rule they are located 2 to 3 cm. from the intestine. Some of these form conical projections; one in particular measures 2 cm. in diameter at its base and 2 cm. in height, is shaped like a nipple and studded with small semi-spherical elevations which give it a lobulated appearance. Some of these mesenteric nodules are pigmented; most of them are not. The tumor masses projecting into the cavity of the lesser omen-

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tum are larger than all other metastatic growths except that in the liver. The larger of these to the left of the vertebræ measures 8 cm. in diameter; it is nearly spherical; that on the right side measures 6 cm. in diameter and is slightly flattened. On section the larger in its outer half consists of many cavities in a brownish tissue. They are generally oval and contain a dirty brown fluid which is turbid. These cavities measure from 2 and 3 mm. to 2.5 cm. in their longest diameters. Some are connected; they give to that part of the mass an areolar appearance. Its inner half on section has the same appearance as the cut surface of the mass on the right of the spinal column, viz., a grayish-white firm surface across which lines extend in various directions. The lines represent the borders of various nodules or islands of tumor tissue which have fused.

Examination of the brain. spinal cord and eye was not allowed.

HISTOLOGICAL EXAMINATION.

Heart Muscle.—The heart muscle fibers contain a large amount of brownish pigment. There is a great variation in the size of the nuclei. There are many leucocytes in the blood vessels of the myocardium. A large proportion of these are the polymorphonuclear variety. There are no bacteria in the blood vessels of the heart that are apparent with the hematoxylin stain as is the case in the pancreas. A number of white bodies implanted on the endocardium of the heart all showed thrombi in different stages of organization. There are no groups of cells found in any of these which could be positively asserted to be tumor cells. The aorta shows no changes.

The mucous glands in the sections of the *trachea* examined, appeared to be hypertrophied. The capillaries of the tunica propria are dilated and filled with blood. The same conditions were found present in the cross-sections of the larger bronchi.

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Sections from the left *lung* show very much distended and in some cases ruptured alveoli and very marked pigmentation about the bronchi and bronchioles with coal pigment. Sections from the lower lobe of the right lung show the changes commonly found in atelectasis.

The *liver* possesses a very good lobular arrangement and the rows of liver cells are very distinct. The staining of the liver cells and nuclei is in all respects typical. The walls of the intralobular capillaries appear thickened and hyaline. There are some small foci of round cells about the intralobular bile ducts and the blood vessels all show an excess of nucleated cells.

The *spleen* shows very marked engorgement with blood, small Malpighian bodies, deposits of blood pigment beneath the capsule and close to the trabeculæ in the deeper parts of the spleen, also slight endarteritis.

Small Intestine.—One of the tumor nodules; the nodule lies in the submucous coat, but also extends into the circular muscular fibers. Alveolation is well marked. Very little pigment has been produced and the tumor cells show signs of considerable compression.

Left Suprarenal Body.—In the medullary portion of the left adrenal are numerous large cells which in their grouping resemble the cells seen in metastatic tumor growths elsewhere. There is no dark brown pigment, however, such as the tumor cells have produced in other locations. On the other hand, there is in these cells none of the pigment usually found in the medullary region of the adrenal; the cells of the adrenal just adjacent to these are pigmented in the usual manner. The line of demarcation between the two is very abrupt.

Lobe of Thyroid.—Sections from the right lobe show very fine acini which contain colloid material. There are rather coarse hyaline bands of connective tissue which separate oval nests of tumor cells or irregular nests with rounded margins. The bands of stroma in places contain large amounts of pigment. The pigment

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is also present in the nests of tumor cells. Alveolation is well marked, many nests of tumor cells being subdivided again and again by delicate strands of connective tissue. The tumor cells are large cells and many contain karyokinetic figures. In places the tumor cells have suffered marked compression and they are very much distorted. Pigment occurs both in the cells and between the cells, but mainly in the latter portion. It is a dark brown color.

Pancreas.—Where the pancreas is uninvaded by tumor tissue there are rather large regions of necrosis, and in the margins of these are numerous bacteria of different shapes. Bacteria are also numerous (mainly bacilli) in the blood vessels and ducts. The regions have all the appearance of a postmortem or agonal necrosis. In regions that are not necrotic, the cells appear to be swollen. The blood vessels in the pancreas possess normal walls.

Kidney.—In the pyramid of one of the kidneys is a small tumor nodule in which alveolation is so marked that in places the groups of tumor cells resemble cross-sections of tubules. Where the pigment is present it is for the most part intracellular. The tumor cells in the center of this growth are small and quite spherical and resemble naked nuclei. As the tumor cells become larger the cell bodies stain intensely with eosin.

In a section of one of the kidneys there is found just beneath the capsule a cluster of cells constituting a so-called adrenal rest; they are disposed in rows, and these rows are frequently double in number, with delicate vessel-bearing strands of connective tissue between them. The rows of cells sometimes form circular or oval bodies, which resemble cross-sections of large tubes. In such are found many cells lying within the space, and sometimes among these the row arrangement is preserved to a slight extent. The cells composing this cluster are of two kinds: 1. A rather large cell with a

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nucleus which stains purple and the nuclear membrane more intensely than the rest of the nucleus. These cells predominate, and where the row formation is most perfect the cell body is distinctly columnar. 2. A cell which is usually smaller, the nucleus more irregular in shape and stains very darkly like a leucocyte. In some places they resemble plasma cells in shape. In the kidney there are some foci of small cells in the cortex, a few fibroid glomeruli, considerable swelling of the working epithelium and engorgement of the capillaries in the cortex. The large blood vessels in the kidney contain bacilli similar to those seen in the pancreas.

The metastatic tumor growths show in all cases the following features in varying combinations:

1. Large fibrous bands which divide the tumor into irregular loculi. These sometimes contain foci of round cells and they are always quite vascular.

2. Delicate bands of fibrous tissue which divide the tumor cells of any one large group into smaller clusters

3. More or less intracellular and extracellular pigment.

4. Karyokinetic figures.

5. Compression so that distorted and flattened cells are frequently seen in the ultimate groups. (The alveolar arrangement of the tumor is very marked.)

6. Regions of necrosis.

7. Areas of hemorrhage.

The position that secondary sarcoma of the liver, especially that form following primary tumor of the eye, occupies in the domains of clinical medicine and of pathological anatomy has been one of gradually increasing importance since the article by Litten in 1889. The loss of an eye or the existence of a tumor of the eye, the appearance of subcutaneous tumors, ascites, emaciation and cachexia with enlargement of the liver, constitute a syndrome that has come to be practically pathognomonic.

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The enlargement of the liver is often greater than in the case reported here; Hamburger has reported one in which the liver weighed 8.3 kilo. and Litten one with a liver of 10 kilo. A very valuable symptom is the presence in the urine of melanin; in some cases this is evident by the black color the urine assumes on exposure to the air for a short time; in other instances it is necessary to add some oxidizing agent.

Valuable additions to the literature of this subject have been made by Hektoen and Herrick (*American Journal of Medical Sciences*, 1898, cxvi, 255), and by Rolleston (*Lancet*, 1899, i, p. 1273, London). The first-named observers emphasize the occurrence of ascites, which they account for by the growth of the tumor cells into the capillaries of the liver and the infiltrating character of the metastatic tumor of the liver. Rolleston has reported a case and summarized 36 cases of melanotic sarcoma of the liver that he was able to find in the literature. Of these the primary tumor occurred in the eye 24 times.

October 12, 1899.

PAPILLOMA OF THE GALL-BLADDER.

E. R. LE COUNT.

The following description concerns a growth that was found in the gall-bladder of the body of an old man 76 years of age. who died from pneumonia.

Abstract from the Necropsy Record.

Biliary Channels.—A small amount of brownish fluid exudes from the duodenal end of the common duct. The gall-bladder is greatly enlarged and distended with a

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large amount of brown bile; it also contains 12 calculi. The smallest of these is the size of a pea, the largest the size of a marble. Attached to the most distal part of the lining of the gall-bladder is a mass of tissue that appears necrotic; its attachment is limited to one place and is made by a very narrow pedicle. The gall-bladder extends 4.5 cm. beyond the margin of the liver; its length over all is 15 cm. The sacculations and tortuosity of the neck appear exaggerated. The contained pedunculated tumor measures 6x4.5x0.5 cm. Its pedicle is no larger than a match. On section the growth appears soft and very bloody.

Microscopic Examination.—The tumor contains very little stroma, but is made up to a large extent of a mass of clotted blood and necrotic tissue in which there are found occasionally, tubules filled with cells and formed by long columnar cells. Some tubules are completely necrotic, others partially so. Blood occurs free and in numerous thin-walled channels, whose general course is parallel. Necrotic areas which stain with eosin and in which the outlines of the cells are still discernible occur, as well as necrotic areas which stain diffusely with hematoxylin; i. e., which contain a greater quantity of nuclear debris.

Sessile polypi of mucous membranes are often transformed into malignant tumors as, for instance, the multiple polypi of the intestine. When, however, the growths are attached by slender pedicles, they are more likely, as was the case here, to become necrotic from some interference with the blood supply.

April 9, 1900.

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EMPYEMA OF THE GALL-BLADDER.

DANIEL N. EISENDRATH.

The case was one of empyema of the gall-bladder, operated upon by Dr. Greensfelder, in a girl 17 years of age, with no symptoms prior to a few days before operation, and even when first examined the clinical picture and local findings greatly resembled those of an appendicitis. The gall-bladder was sutured to the abdominal wall, and after two days was opened. Seven gallstones and a large amount of pus containing the colon bacillus in pure culture were evacuated. Shortly after operation the patient became jaundiced and died within forty-eight hours with all the symptoms of cholemia. Autopsy showed a gallstone impacted in the opening of the cystic duct, a plug of mucus at the duodenal orifice of the common duct, and a most extensive yellowish discoloration of the liver, which microscopically showed coagulation necrosis in the center of the lobules, and considerable round-cell infiltration along the smaller bile vessels. The production of the cholemia in this case was in all probability due to two factors, obstruction to the common duct and the infectious cholangitis, etc. There was no evidence of post-operative infection.

November 13, 1899.

ANNULAR PANCREAS.

THEO. TIEKEN.

Opinions differ somewhat in regard to the early development of the pancreas, though all agree that it is de-

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veloped from that part of the primitive foregut which later becomes the duodenum. His,[1] in specimens of human embryos, about the fourth week, found two dorsal outgrowths from the intestinal canal, nearly opposite the ventral diverticula which form the liver; Hertwig and others agree with his views. Minot[2] thinks it is formed from a single dorsal diverticulum which grows backwards into the folds of the mesentery. Stoss[3] claims that there are two pairs of diverticula, two ventral and two dorsal. Felix[4] has studied carefully the sections from embryos of the chick, cat, and two series from human embryos, and comes to the following conclusions: In the chick there are three diverticula, one dorsal and two ventral, all of which take part in the development of the organ. In the cat, one ventral and one dorsal, both of which take part in the development of the gland. In the human embryo there are three diverticula, one dorsal, one left (rudimentary) and one right ventral diverticulum. The two ventral fusing together, form the true pancreatic duct, while the dorsal remains and forms the duct of Santorini.

All agree, too, that the diverticula are at first solid processes, which later on become hollowed out, and in this way the ducts and tubules are formed. The processes grow out from the intestine, and, as they enter the mesoblastic tissues surrounding the gut, they receive a covering from this layer, which forms the capsule and grows into the gland structure, dividing it into lobules, thus forming the connective tissue framework. The pancreatic diverticula appear a little later than the hepatic, and are almost directly opposite the latter, usually being a little below the ventral hepatic diverticula. As growth takes place, the ventral and dorsal pancreatic processes join and form the fully developed gland.

At first the pancreas lies in an antero-posterior direction,[5] but the gland soon assumes a transverse position, its tail being towards the left, while the head follows the

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duodenum and turns towards the right side. It is covered by the mesentery, being enclosed by the two layers of this structure during its early period; but, as fusion of the mesogastrium and the transverse mesocolon occurs, the posterior layer of the mesenteric fold is absorbed, and it now lies apparently behind the peritoneum along the back of the abdominal cavity.

At the beginning the pancreatic and hepatic ducts are entirely separate and occupy opposite sides of the duodenum, but, as growth takes place, the ducts gradually approach each other and finally become fused, forming the common duct, which opens into the intestine by a single opening at the ampulla of Vater. If for any reason this fusion does not occur. we have an abnormality of the pancreatic ducts;[4] many varieties of this anomaly have been described; they are not at all uncommon. We may have two pancreatic ducts; the duct of Santorini entering separately, or both ducts may enter the duodenum by independent openings, without joining the hepatic duct. In one case, the duct of Santorini entered the stomach.

If development proceeds without fusion of the separate diverticula we have formed the accessory pancreas,[6] which is one of the most frequent abnormalities of pancreatic development. Fourteen cases have been reported up to date. Klob[7] was among the first to report cases of this variety, and was the first to give a full microscopic description of accessory pancreas. Since his cases were published Zenker,[8] Wagner,[6] Gegenbauer,[9] Neuman,[10] Nauwerck,[11] Nicholls[12] and Glinski[6] have reported similar cases. The position of the accessory gland is quite variable. It has been found in the walls of the stomach and duodenum; in the mesentery and in the diverticula of the jejunum, as far down as the ileo-cecal valve. The variations in size have been given from 2 millimeters to 3 centimeters in diameter. and the form is also quite variable. In one instance, two acces-

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sory glands were found; one 48 centimeters and the other 60 centimeters from the duodenum (Zenker[8]).

The importance of the accessory gland in causing diverticula of the intestine has been suggested by some writers, and the fact that it has been found in the very tip of such processes renders it not improbable that it may have had something to do with their formation.

The third abnormity described is the "pancreas minus" of Winslow, which is merely a small accessory pancreatic lobule, springing from the head of the main gland, usually extending along the wall of the duodenum.

A fourth variety, described by Hyrtl,[13] consists of a partial division of the body of the gland by the mesenteric vessels. To this variety he applied the name "pancreas divisum," on account of the separation of the gland substances, by pressure from the vessels during development.

A fifth variety,[14] which can scarcely be called an abnormity of development, is one in which there is an hypertrophy of the glandular substance about the head, which extends from the head and partially surrounds the intestine. Sometimes the circle is completed by a band of fibrous tissue, which connects the two glandular processes, when it approaches the type which is the subject of this paper—namely, the annular pancreas. Genersich,[14] described several cases of this kind in which there was some constriction of the intestine, and above it, some dilatation of the duodenum.

The sixth and most important abnormity is a very rare condition, first described by Ecker,[15] in 1862, who gave it the name it now bears—"pancreas annulare." In the literature I have been able to find but four cases described, and a notice that another specimen had been exhibited, but no description is given.

Ecker[15] described his case as follows: "A band-like extension was noticed springing from the head of the

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gland, on either side of the intestine, and these outgrowths joined on the opposite side, forming a complete circle about the lower portion of the descending duodenum. A duct was found, originating in the annular portion, which gave off many small branches, entering the glandular substance. This duct approached that of the main portion of the gland, but did not empty into it." He does not state where it terminated, or if it emptied into the duodenum by an independent opening, nor does he say anything about the effect produced upon the stomach or intestine. Judging from the illustration, it seems that the duodenum above the constriction was larger in diameter than that below, so that some narrowing may have been caused by the annular band.

In Auberg's[16] case, quoted by Ancelet in 1866, the duodenum was surrounded by the main body of the gland, which seems to have been considerably enlarged. There was some narrowing of the duodenum, but the description is not very clear. No mention is made of any change in the stomach.

Symington[17] reported a case in 1885, and described it as follows: "The lower part of the descending duodenum was surrounded by a complete band of pancreatic substance, which originated at the upper part of the head and extended on either side of the intestine, meeting at a point opposite its origin, where it measured one half inch in vertical diameter at its narrowest portion. The circumference of the duodenum at its constricted part measured only two and one-half inches, while that above was at least three times as large. The part below the constriction was also considerably enlarged." No description is given of the stomach, as only the duodenum was examined.

Genersich[18] (1891) reports the fourth case of annular pancreas and gives a very comprehensive description of the anomaly. In a postmortem examination of the body of an adult male subject he found, just below the

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pylorus, a swelling, which was about the size of an apple, somewhat movable laterally and quite firm to the touch. Upon removing the omentum, this was found to be the head of the pancreas, greatly enlarged and completely surrounding the duodenum. The neck of the gland was quite small and joined the normal body to the head, which, as stated, was unusually large, and measured, after removal, 6 centimeters in a vertical direction and 7 centimeters transversely. The annular portion, which was an outgrowth from the head, had the following dimensions: At the beginning, 3 centimeters broad, becoming gradually narrower, until it measured only 1.5 centimeters broad and 0.8 centimeter thick. The annular portion measured 4.5 centimeters in its entire circumference; the narrow portion measuring only 3 centimeters. The annular portion contained a very large branch from the pancreatico-duodenal artery, and also a large vein, which emptied into the superior mesenteric. The hepatic and cystic ducts joined in the posterior part of the annular band, and were later joined by the pancreatic duct, all emptying in common at the usual place into the duodenum. Where the duodenum was surrounded, a constriction obtained, which admitted the tip of the thumb with difficulty, and measured only 6 centimeters in circumference. The duodenum above the constriction was greatly dilated, and approached in size the large intestine. The pyloric opening was dilated, and the stomach both dilated and hypertrophied. Below the constriction the duodenum was slightly narrower than normal. There were rather loose adhesions between the intestine and the annular part of the pancreas, so that some degree of mobility was obtainable. The structure of the constricted portion of the duodenum was not altered. In this case, then, there is in addition to the malformation of the pancreas, a constriction of the duodenum, dilatation of the part

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above, dilatation of the pylorus and dilatation with hypertrophy of the stomach.

Dr. Hugo Summa,[19] of St. Louis, Mo., exhibited a specimen of annular pancreas at the annual meeting of the American Medical Association, at Atlantic City, N. J., 1900, but I could not find any detailed description of this case in the literature.

The case now to be described concerns a true annular pancreas, causing constriction of the duodenum with sacculation of the intestine above the narrowed portion, dilatation and hypertrophy of the pylorus, and hypertrophy of the wall of the stomach. This case occurred in a man, 34 years of age, janitor by occupation, whose family history was of no special significance. He had been a constant drinker of alcoholics in moderate amounts and had had rheumatism, gonorrhea, pneumonia and numerous other minor ailments before admission to the Cook County Hospital, May 22, 1900, in the service of Drs. Billings and Preble, where he was under constant medical observation for ten months previous to his death. He was subject to frequent and thorough examinations, but never gave any evidence of gastro-intestinal disturbance of any kind, complaining only of the cardiac symptoms, from which he suffered. After a severe attack of facial erysipelas the cardiac symptoms grew rapidly worse and death occurred after one week's illness.

Anatomical Diagnosis: Acute endocarditis of mitral and aortic valves, with ulceration of aortic valves and perforation into the peri-aortic space; fibrinous pericarditis; passive hyperemia of liver and spleen; old and recent splenic infarcts; annular pancreas; constriction with sacculation of the duodenum; hypertrophy and dilatation of the pylorus; hypertrophy of the stomach, and general arterio-sclerosis. Unfortunately, the exact anatomical relations of the pancreas were not studied,

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because the anomaly was not discovered until nearly all of the abdominal viscera had been removed.

After removal from the body, the pancreas, duodenum and stomach were carefully examined, with the following result: The head of the gland is somewhat enlarged, measuring 3.5 centimeters in its transverse and 4 centimeters in the vertical diameter. The neck is about normal in size and joins the normal-sized body to the head in the usual manner. From the head two broad bands of glandular substance extend forward in such a manner as to surround the lower part of the descending duodenum, forming a complete ring about its circumference. At the base these bands measure nearly 4 centimeters in their vertical diameter and gradually become narrower until they join on the opposite side of the intestine, where they measure 2.75 centimeters in breadth by 1 centimeter in thickness. The duodenum is greatly constricted at this portion and admits the tip of the index finger with difficulty. There are some rather loose adhesions binding the duodenum to the annular band, but some motion is obtainable. A careful dissection was made of these parts. After separating the adhesions between the duodenum and pancreas, a considerable degree of mobility is obtained. The pancreatic duct opens into the intestine at the upper part of the annular band. It is joined by the hepatic duct, and the two open in common in the usual manner. Nothing abnormal is found in the vascular supply, and sections cut from the head, body and annular portion show the tissue to be normal pancreatic substance. The neck of the gland measures 2.25 centimeters in diameter; the body 15 centimeters in length, 2.5 to 3.5 centimeters in breadth, and 2 to 2.5 centimeters in thickness. On sectioning this portion nothing abnormal is seen. The gland is of about normal consistency and shows the usual lobulations. The splenic vein is con-

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siderably dilated and the splenic artery somewhat sclerotic.

The duodenum above the constriction is greatly dilated, forming a sacculation nearly one-half the size of the stomach. The wall of the dilated portion is thin in the convex part, but the muscular layer of the concave surface is somewhat hypertrophied, the fibers standing out prominently where the serous coat has been stripped off. The dilated portion measures 10 centimeters along the upper concave and 20 centimeters along the lower convex border; 28 centimeters in its greatest circumfer ence when distended and 9 centimeters in diameter. Below the constriction the duodenum is of about normal size.

The pylorus is greatly thickened and the opening enlarged, measuring 4.25 centimeters in its external diameter.

There is no marked dilatation of the stomach, but the muscular coats are greatly hypertrophied, especially in the pyloric half. It measures 11 centimeters along the lesser, 37.5 centimeters along its greater curvature, 11 centimeters from above downwards at its middle, and 30 centimeters in its longest transverse axis.

In summing up the conditions, it is evident that the changes found in the stomach and duodenum have been caused by the narrowing of the lumen of the intestine, due to the annular band of pancreatic tissue, which surrounds the descending duodenum.

The chief points of difference between this case and those previously reported are as follows: 1, the more extensive dilatation of the duodenum above the constriction; 2, the greater narrowing of the lumen of the bowel; 3, the more extensive development of the annular portion of the gland; 4. the absence of dilatation of the stomach; 5, the greater hypertrophy and dilatation of the pylorus.

In regard to the genesis of annular pancreas, the fol-

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lowing is suggested: If the ventral and dorsal diverticula did not unite as they normally do, but each developed independently, there would be pancreatic tissue on either side of the intestine, and as growth proceeded the bowel would soon be completely surrounded by glandular tissue. In the semi-annular type the condition might be due to an overdevelopment of the head, which send out processes, partially surrounding the bowel. If this hypertrophy should continue until the processes meet on opposite sides of the duodenum there would be a true annular pancreas, and there is no reason why this could not occur.

As regards the clinical significance of the pancreatic anomalies referred to in the foregoing, then it would seem that the pancreas minus and divisum. the accessory pancreas and the malformations of the ducts, always interesting from an anatomical standpoint, are of little practical importance to the diagnostician, as they can not be detected during life, nor do they bring about pathological conditions of a serious nature. According to Opie,[20] anomalies of the ducts may be a factor in causing hemorrhagic pancreatitis from impaction of gallstones in the ampulla of Vater, as shown by the case examined by him recently.

The accessory pancreas may be a factor in the production of diverticula of the intestine (Glinski) or perhaps it might become the seat of tumor formation, when it would be of considerable pathological importance.

The "semi-annular" type, according to Genersich, is of some practical importance, because it is capable of producing duodenal constriction.

The annular pancreas, however, is capable of producing changes which may become of great importance. as was stated above. In the present case the obstruction of the bowel is marked and has led to great dilatation of the duodenum. It is easy to understand the conse-

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quences that would ensue if, in a similar case, the obstruction should become more marked.

Should there develop a tumor of the head of the pancreas, as carcinoma, for instance, there would be early stenosis of the bowel, and probably occlusion of the bile ducts as well. In case of operation the condition would puzzle the surgeon, who might think he had to deal with a so-called "hour-glass" contraction of the stomach.

The accumulation and decomposition of food in the duodenal sacculation may be mentioned as another possibility, from which serious symptoms would arise. Hence, annular pancreas is of interest from a practical as well as a pathological standpoint, and should be taken into consideration in all obscure instances of tumor and obstruction at or near the pylorus.

March 11, 1901.

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SARCOMA OF THE PANCREAS.

GEORGE A. BOYD.

Litten[1] was the first to report a primary sarcoma of the pancreas in which the microscopic findings were recorded. His case occurred in a boy 4 years old. The tumor weighed fifteen pounds. Virchow made the microscopic examination and found a small round-celled sarcoma. This was in 1889.

Senn,[2] in 1886, reported two cases of sarcoma of the pancreas; one from Mayo's "Outlines of Human Pathology," published in 1836. As this was probably the first case of primary sarcoma of the pancreas it will be given with some detail. Quoting[3] from the original work:

Malignant disease rarely attacks the pancreas alone, but involves in common with it either the stomach or liver or both.

A gentleman, aged 35, died after an illness of about eighteen months' duration in which it was to the last impossible to say what organ was the seat of the disease. His complaint began with a febrile attack which left him weak and from that time he was liable to dyspeptic symptoms with variable appetite and an undefined uneasiness in the epigastric region. He gradually lost strength and flesh and when he consulted Dr. Newbegging in January, 1822, he was found thin and weak; but Mr. N. was particularly struck with his remarkable paleness, even his lips and the inner surface of his mouth was entirely without color. About this time he had some vomiting and was feverish for a day or two. . . . When I saw him in April he was reduced to the last degree of paleness and debility, but his pulse was full, strong, and regular. . . . He died at the end of April without any change of symptoms except that his pulse became frequent a few days before his death.

Inspection.—All of the internal parts were found remarkably pale and void of blood; the heart was sound, but remarkably empty. The pylorus was thickened and firmer than natural and had contracted an adhesion to the pancreas. The pancreas was considerably enlarged and of nearly cartilaginous hardness except some spots which were soft with the appearance of the medullary sarcoma. No other disease could be detected in any other part of the body.

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The histologic character of this tumor must remain unknown. Its history does not exclude carcinoma.

Senn reports a case of Lepine and Cornil[4] which occurred in 1874.

In 1880 Bartley[5] reported a case of spindle tumor of the pancreas, to the New York Anatomical and Surgical Society. The tumor occurred in a farmer 22 years old. The tumor began, it was supposed, six years before his death, at which time he suffered from epigastric pain at the time ascribed to a strain. Two years later the pain returned and occurred with constantly shortening intervals until the pain became continuous. One year and a half before his death he consulted a physician and was treated for gastralgia, cardialgia and dyspepsia. In the fall of 1879 he came to Chicago to seek medical aid. He died one month later and the necropsy showed tumor of pancreas adherent to the stomach, splenic vein, hepatic gastro-duodenal arteries. The lymph nodes along the aorta were enlarged. The head of the pancreas was the "size of the fist" and the tail the "size of the wrist." The tumor was firm in consistence and microscopically was a spindle-celled growth. The reporter, while recognizing it as probably sarcoma, reports it as carcinoma. The age of the patient supports the diagnosis of sarcoma, which no doubt it was.

In 1892, Mansilla[6] reported a case occurring in a man 54 years old. Microscopic examination showed "embryonic sarcoma" of the pancreas, with metastatic deposits of the same character in the liver.

Primary sarcoma of the tail of the pancreas in a man 74 years old. with metastases in the liver and peritoneum, was reported by Blind[7] in 1894.

Ehrmann,[8] in 1896, reported a case of primary sarcoma of the tail of the pancreas in a woman 56 years old, with metastases in the liver and pleura.

Picola[9] is generally credited with two cases, a distinc-

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tion he did not claim. He states that in one the primary growth was in the liver and the pancreas was involved secondarily. The case he reports as primary sarcoma of the pancreas occurred in a man 54 years old. There were three small tumors in the head of the pancreas, the largest one the size of a walnut and the others the size of peas, their surface smooth and pink in color. On section, the color was gray. There were adhesions with the hilus of the liver, with the intestines and metastases in the abdominal lymph nodes. The bile-ducts were dilated and the alveolar epithelium necrotic.

Churton[10] reported a round-celled sarcoma of the pancreas. The connective tissue of the pancreas was infiltrated with small round cells, and the lobules invaded. There were metastatic deposits in the liver and adhesions between the pancreas, left kidney and the spleen. In this case there was glycosuria.

Neve[11] met with a case in a man 64 years old. The growth involved the pancreas and pylorus. It was firm, yellow and on section glistening and fibrous with small areas of darker color. It looked like a scirrhous carcinoma. The microscope showed it to consist of "highly nucleated" spindle cells interlacing at all angles. There were no epithelial cells.

Schueler,[12] in 1894, reported a case in a man 38 years old. The patient was an alcoholic. He vomited and suffered pain in the cardiac and costal regions. There was pain on pressure over the xiphoid process. Eating caused the pain to grow worse. Palpation showed a tumor the size of an egg in the left part of the liver. Exploratory puncture showed a reddish-brown fluid. Autopsy showed a large cystic tumor of the pancreas containing 2 liters of brown fluid. In part of the pancreas, not cystic, there was a large spindle-celled sarcoma. Metastases were found in both pleuræ and the third and fifth dorsal vertebræ. In this case there was no free hydrochloric acid found in the stomach.

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The Spanish have another case, reported by Machado[13] in 1883.

Aldor,[14] in 1895, reported a "medullary sarcoma" of the pancreas in a man 45 years old. The tumor was the size of a man's fist and had perforated into the stomach and was adherent to the spleen and duodenum.

Frohwein[15] reported a case in 1897, of a spindle-celled sarcoma of the pancreas.

Ehrmann[16] described a case of primary sarcoma of the tail of the pancreas with metastases in the liver and pleuræ. Both the primary neoplasm and the metastases were of the small round-celled type.

Italia[17] reports the most recent case found recorded. The tumor occurred in a man 70 years old. The first symptoms were noticed in February, 1899, and death occurred in September following. The tumor was about the size of an orange and painful on pressure. Diagnosis was made in this case during life. The autopsy showed a large amount of peritoneal effusion. The tumor of the pancreas was round but distinctly limited. Metastatic nodules were found in the liver. The tumor in the pancreas was a small round-celled sarcoma, while the deposits in the liver were of the large-celled variety. The pancreatic tumor was considered the primary growth.

In the seventeen cases summarized, three may be questioned, two of them, Mayo's and Bartley's, because the evidence of sarcoma is not complete and one reported by Schueler might have been secondary to the tumor growth in the vertebræ. They have been included in the list of primary sarcomas because it is more probable that they belong there than in the seriously questioned list.

There are tumors reported as primary sarcoma of the pancreas where the evidence is incomplete.

Paulick's[18] case, generally included among the recorded cases of primary sarcoma of the pancreas, oc-

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curred in a young man who died of pulmonary and intestinal tuberculosis. The tumor gave rise to no symptoms, yet it is reported as a round-celled sarcoma. The question as to whether this was a tuberculous pancreas does not appear to have occurred to the reporter.

Briggs[19] reported a case in 1890 occurring in a woman 45 years old. The tumor was a cyst filled with two liters of grumous dark fluid in which were found the hooklets of the echinococcus. The tumor was removed, and the patient recovered and remained well at the time the report was made. The period elapsed since the operation was not given. The tumor was reported as "sarcomatous," with no microscopic detail.

Billroth and Bozeman are both credited with a case of sarcoma of the pancreas, but the conditions found were cysts, not sarcomas. Ehrmann included in his list a case reported by Bruen[20] in 1883. He describes a colloid tumor of the head of the pancreas, but gives no microscopic report.

Chiari[21] reports a metastatic growth in the pancreas occurring secondary to a sarcoma in the eye. This case has been included in reports, but should be excluded from the cases of primary sarcoma. Some cases not reported as sarcoma of the pancreas are worth reviewing because they lead to the conviction that they were sarcoma. If sarcoma has not been recognized in these cases it may not be its absence so much as a failure to properly diagnose the tumors of the pancreas that has made it so rare that Ziegler states that "they are extraordinarily rare," Orth that "they are almost unheard of." Hamilton is silent and so is Delafield and Prudden, while Stengel gives the subject three lines in his latest work.

Pepper,[22] in 1871, reported a case of tumor of the head of the pancreas in a man 45 years old. Necropsy showed a cyst the size of a walnut, filled with blood, the cyst cavity trabeculated with fibrous bands and lined with smooth mucous membrane. The cyst communi-

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cated with the duodenum. The microscope showed the acini of the glands diminished in size and the "epithelium in the state of granular degeneration" with an abundance of oil globules. "After the fat was dissolved out with sulphuric ether and acetic acid was added, an immense number of elongated nuclei attested its vigorous nutrition and growth." The fact that the growth was not in the epithelial structures, and that the nuclei were elongated is very suggestive of sarcoma.

Dieterich,[28] in a report of 145 cases of melanotic tumors, in 1887, mentioned a case of sarcoma in a child 2 years old. There is no report of a microscopic examination.

REPORT OF CASE.

The case which is here added to the list of primary sarcoma of the pancreas, occurred in the practice of Dr. M. L. Harris. The patient entered the Policlinic Hospital, Nov. 16, 1898.

History.—N. B., aged 47, a male, was a driver of a coal wagon. His father died at the age of 60, the cause unknown, his mother at 64, the cause unknown. Two brothers were living and well, also one sister. The patient used alcohol lightly, but no tobacco. His health was good until June, 1898, when pain appeared to the left of the median line a little below the umbilicus. He felt a lump the size of a large apple and rather firm, which increased in size. His bowels were regular. There was no history of an injury. At the time of entering the hospital he vomited two or three times a week. The vomit was sour at times. His weight had fallen from 165 to 140, and he had lost much in strength, and then had a tendency to constipation. His pulse was 70, temperature 99 F.; respirations 20. At the time of admittance the urine was of straw color, aromatic in odor, with an acid reaction, a sp. gr. of 1028, no albumin, no sugar, no casts. His abdominal measurements were as follows: Maximum circumference, 95.3 cm.; circumference at umbilicus, 94.6 cm.; circumference at crest, 91 cm.; from maximum circumference to ensiform cart., 11.7 cm.; from umbilicus to ensiform cart., 16 cm.; from maximum circumference to symphysis, 20.5 cm.; from umbilicus to symphysis, 16.5 cm.; from umbilicus to ant. s.s. proc. (l.) 22.7 cm.; from umbilicus to ant. s.s. proc. (r.), 22.3 cm.; from max. circum. to

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ant. s.s. proc. (r.), 24 cm.; from max. circum. to ant. s.s. proc. (r), 24.5 cm.

On November 23, an exploratory laparotomy was made by Dr. Harris, and an inoperable large tumor of the pancreas found. The patient gradually lost, his pulse and respirations gradually increasing in rapidity, while the temperature was many times subnormal up to a short time before death, when it ran up to 103 F. The autopsy made by Dr. Herzog was from necessity very incomplete, no regular autopsy being permitted; the body had to be shipped immediately.

The tumor, after having been removed from the abdominal cavity, was irregularly quadrilateral in shape and measured 17 cm. transversely, 20 cm. anteroposteriorly, and 24 cm. in the vertical diameter. Its vertical circumference was 72 cm., the transverse 71 cm. Its walls were firm, pale, slate-colored, mottled and irregularly lobulated. The whole tumor was covered with thickened peritoneum, except when stripped off by attachments to the stomach, spleen and liver, and where it was applied to the transverse colon between the layers of the transverse mesocolon. Posteriorly it was not adherent to any of the large blood-vessels or to the kidney. There was a depression on the upper right posterior surface of the tumor, as if made by the liver. The posterior layer of the lesser omentum was folded over the tumor, giving it the complete peritoneal covering. At no point was the tumor fused with the structures to which it was attached by peritoneal adhesions. The transverse colon was attached along the entire anterior inferior border of the tumor, but the gut walls were nowhere invaded by the tumor growth. When the tumor was cut open it was found to contain in its interior a cavity 13 by 11 by 10 cm. The cavity was subdivided into two compartments by a septum formed by the tumor tissue. The roof of the lower compartment and the internal surface toward the left side were perfectly smooth. Most of the right internal surface and most of the floor were uneven and covered with a ragged grumous mass. Here the tumor tissue had broken into the smooth internal lining of the cyst. The upper compartment of the tumor cavity had evidently not originated as a true cyst, like the lower compartment. It was an irregular pyramidal cavity with a very ragged and irregular internal surface. The cavity was partly filled with broken-down tumor tissue. The tumor wall surrounding the central cavity in varied thickness from 5 to 10 cm. The tumor tissue on section appeared divided by connective tissue trabeculæ into roundish and oval nodules varying in size from a fraction to several centimeters in diameter. Near the outer surface the tumor tissue was grayish-white and quite solid; more toward the interior it assumed a light dirty brown, was spongy and honeycombed. The transverse colon, as stated

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before, was firmly attached to the anterior lower aspect of the tumor. When cut open the gut showed an intact mucous membrane, the tumor not having involved the walls of the gut.

The microscopic examination showed that when the tumor had not undergone any retrograde or degenerative changes it consisted of large spindle cells. These cells took their origin from the adventitia of vessels. The cell nuclei were generally fusiform, some decidedly rod-shaped, others oval and even round. They generally contained one or two nucleoli and a moderate amount of finely granular chromatin. The cell protoplasm was quite abundant and stained deeply with eosin.

The tumor cells formed bundles and masses which interlaced each other freely in every direction. Thin-walled blood-vessels were abundant. At some distance from the surface the tissue exhibited a tendency to retrograde changes. Here the cells showed coagulation necrosis, and the nucleus became indistinct, likewise the cell body. Deeper still the nuclei disappeared and a rarefied tissue was formed which looked like myxoid tissue. In such necrotic places extravasated blood was found free between the degenerating tumor tissue.

The grumous material found in the interior of the tumor consisted of necrotic cells mixed with free decomposing blood, fibrin and hematoidin granules. In some places the necrotic tissues showed numerous polynuclear leucocytes, some exhibiting nuclear fragmentation. One of the pieces of tumor examined showed where the tumor had been attached to the wall of the stomach. The viscus wall was thin and atrophic.

The capsule of the tumor consisted of coarse connective tissue fibers with slender, fusiform, deeply-staining nuclei. No endothelial cells were seen on the capsule.

The kidney showed marked congestion of all the vessels. The epithelium lining the uriniferous tubules showed cloudy swelling. Many of the tubules were filled with a granular material and some contained hyaline casts. The interlobular connective tissue of the liver was moderately increased. The peripheral cells of the lobule were fairly normal, but in the central zone they were densely filled with bile-coloring matter. Both in the peripheral and central zone a number of liver cells showed cloudy swelling. The spleen pulp was densely crowded with erythrocytes. In such places hemosiderin was found in large amounts. In other places the pulp cells showed a tendency to become fusiform. The myocardium was normal.

From the microscopic examination it was evident that we were dealing with a malignant connective tissue tumor—a sarcoma. The neoplasm, as appears from the history, grew rapidly, and speedily led to a profound cachexia. While the tumor formed adhesions to several

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of the neighboring organs it had not broken through any of them, nor had it given rise to metastases. The absorption of the ptomains had produced a chronic splenitis and changes in the liver, partly parenchymatous, and partly indicative of early interstitial cirrhotic changes.

I here express my gratitude to Dr. Herzog for his assistance in preparing this report.

November 12, 1900.

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DISCUSSION.

DR. HEKTOEN—In Vol. II of the Transactions of this Society there is recorded a probable primary sarcoma of the tail of the pancreas. A short time ago, Dr. McLean, of Maroa, Ill., sent to my laboratory a very large cystic round-cell sarcoma, weighing 2300 grams, which seemed quite clearly to spring from the pancreas. No trace of the pancreas was found after thorough search, the organ being wholly replaced by the tumor.

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INTERSTITIAL PANCREATITIS IN CONGENITAL SYPHILIS.

A. P. CONDON.

The to be described case occurred in a small child, delivered at the eighth month, and living but a few minutes. It weighed but four pounds. The skin was drawn and wrinkled, and of a muddy blue color. There was a macular eruption upon the skin, extending over the entire body, and several superficial ulcers upon the abdomen.

The mother of the child was 22 years old, healthy, and had been married four years. She had one child, which is alive and healthy, two years and a half previous to the birth of this one. She did not know of any venereal infection, but stated that she had had an eruption over the arms and chest a year and a half ago; but she thought it was due to ivy poisoning. Her inguinal and cervical lymphatic glands were somewhat enlarged, and the epitrochlear glands were palpable.

The father was 26 years old, strong and healthy; he had syphilis six years ago, followed by one month's treatment.

At the autopsy, made in the Pathological Laboratory of Rush Medical College, sixteen hours after death, the abdomen was found distended with a thin, bloody fluid. The liver was greatly enlarged, and dark red in color. On the surface of the right lobe, and also extending through the substance, were numerous areas of gummous infiltration varying in size from a small pea to a walnut. The connective tissue was uniformly increased throughout the organ. The spleen was enlarged, congested, and the connective tissue increased. In the kidneys no naked-eye changes were noted; but microscopically a number of submiliary gummas were found. The

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connective tissue of the adrenals was greatly increased. The lungs were heavy; did not crepitate; and cut with increased resistance. The cut surface was granular, mottled, and grayish-white in color. There was an increas in the interalveolar connective tissue, and the vesicles were mostly in the state of atelectasis; the vesicles that were partly distended were filled with a granular detritus.

In the thymus was found interstitial hyperplasia and gummous infiltration. In the femur there was no center of ossification in the lower epiphysis, and the line of junction of the epiphysis with the shaft appeared as a light yellowish, irregular zone, three millimeters in thickness.

The pancreas was about normal in size, firm in consistency, and cut with increased resistance. Microscopically there is an enormous increase in the connective tissue which is very rich in cells. It contains young blood vessels, which are distended, and in many places blood has extravasated into the connective tissue spaces. The connective tissue hyperplasia has compressed the lobules and in many places has caused them to disappear almost entirely. The connective tissue increase has caused the parenchyma of the lobules to assume one or more of three forms.

1. The hyperplasia is interacinous, compressing and encapsulating from one to three or four acini with heavy bands of young connective tissue, the area resembling in structure scirrhous carcinoma.

2. The connective tissue penetrates between the cells of the acini, causing them to lose their alveolar appearance, and forming regular, heavily encapsulated masses of cells resembling much the glomeruli of the kidney. Some of these glomerular-like bodies are composed mostly of cells more or less spindle in shape (intertubular cell masses of Langerhans).

3. The connective tissue increase has caused the dis-

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appearance of all of the parenchyma, excepting the small branching pancreatic ducts, which appear as short, wavy parallel rows of cells. The walls of the blood vessels are thickened.

Syphilis of the pancreas is rare in the acquired form. Peterson found only one case in eighty-eight that died during the tertiary period of the disease. In the congenital form it is more frequent. Schlessinger, in an article in *Virchow's Archives* (vol. 154, page 501), has carefully gone over the literature upon the subject, and finds that the pancreas is not affected as often as the spleen, liver, lungs and bone; but more frequently than the thymus, heart, intestines and kidney. Syphilis attacks the pancreas in two forms: the diffuse interstitial pancreatitis and the gummous infiltration. Macroscopic gummas in congenital syphilis are very rare in the pancreas, only two cases having been reported, one by Klebs and one by Beck. Microscopic gummas are also rare. In the interstitial pancreatitis the hyperplasia usually commences in the walls of the blood vessels, sometimes in the walls of the ducts. It usually begins in the head of the pancreas. The process causes the organ to increase in size, and in consistency, sometimes to the extent of becoming as hard as cartilage. The newly-formed connective tissue encroaches upon the parenchyma, producing pressure atrophy. The pancreatic ducts are not easily destroyed, and are usually visible after the destruction and disappearance of the acini. The intertubular cell masses of Langerhans, which are found more frequently in children than in adults, are usually not affected, either by the interstitial hyperplasia or atrophy of the parenchyma. There are usually no degenerative processes accompanying this condition. So far the changes described in the pancreas have not been brought into relation with diabetes; and it seems to me that this would be an interesting point to investigate.

February 12, 1900.

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A CASE OF CIRRHOSIS OF THE LIVER AND OF THE PANCREAS, WITH DIABETES AND HEMACHROMATOSIS.

A. P. CONDON.

The patient, a man, white, aged 42 years, was brought into the Cook County Hospital by the police May 25, 1899, in a semi-comatose condition. He gave a history for one year previous of the symptoms of diabetes, such as thirst, polyhagia, glycosuria and pruritus, but the exact details were not obtainable. He died in coma the following day. He had no friends or relatives, consequently his past history could not be obtained.

The postmortem examination twenty-four hours after death revealed the following: The body is that of a fairly well-nourished man. The extremities are somewhat emaciated and the chest is decidedly barrel-shaped. Postmortem rigidity is well marked. The integument covering the whole body is of a yellowish-brown color.

In the peritoneal cavity there are adhesions between the right lobe of the liver and the anterior abdominal wall. The left lobe of the liver is free. The parietal peritoneum and the serous surface of the intestines show a uniform yellowish-brown pigmentation. The intestines are free from adhesions, except the tip of the appendix, which is embedded in a mass of adhesions behind the cecum between this and the abdominal wall. The diaphragm reaches to the fourth intercostal space on the right side, and to the upper border of the fifth rib on the left side.

The lungs overlap each other in the median line. The left pleural cavity is empty; the right pleural cavity is obliterated by easily broken-down adhesions. The lungs float and crepitate. The upper lobes are lighter in color and contain a small amount of coal pigment. The lower

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lobes are of a dark-red color, a frothy fluid exuding upon pressure. The right interlobar fissure is obliterated by adhesions similar to the adhesions in the right pleural cavity.

The layers of the pericardium are adherent, and the cavity contains a small quantity of slightly cloudy fluid. The parietal pericardium is covered with a network of small vessels engorged with blood. The heart weighs 285 grams, is softer than normal, and is of a pale brown color. The aortic and pulmonary valves are competent. The anterior cusp of the mitral valve is thickened at its base. The foramen ovale is open.

The liver weighs 2700 grams. The surface is of a mottled brownish-yellow color and uneven, due to small nodular elevations. The capsule is much thickened and the consistence is increased. Upon section the same mottled appearance is evident. There is a decided increase in the fibrous stroma and the lobules appear distinct, being lighter than the stroma around them. The gall-bladder extends beyond the liver; it is distended by a thick, dark bile.

The spleen is enlarged, measuring 13x8.5x3.5 centimeters. The capsule is thickened, and upon the diaphragmatic surface are whitish nodules. Upon section, the spleen is grayish in color, and the connective tissue trabeculæ are relatively increased.

The stomach contains a large amount of bile-stained mucus. The mucous membrane of the intestines appears normal.

The pancreas is larger than normal and cuts with increased resistance. The cut surface shows brownish-yellow pigmentation, and a marked increase in the fibrous stroma.

The capsule of the kidneys strips easily; upon section, there is an increased amount of blood, the color is dark red. the cortical markings are distinct, and the glomeruli are plainly visible.

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Bacteriological Examination.—The cultures from the lung gave the bacillus coli communis and the pneumococcus; from the heart's blood, the staphylococcus pyogenes albus; from the pericardial cavity, the pneumococcus; from the liver, the kidney, and the spleen, the bacillus coli communis was obtained. The tubes inoculated from the pancreas were sterile.

Histological Examination (after formalin-alcohol fixation).—Lungs: A number of the acini are filled with a homogeneous material, which stains pinkish and contains no cells. Some of the acini which are not filled with this fluid are seen to be widely dilated, and some of them are ruptured. The vessels are distended with blood and a heavy deposit of black pigment surrounds them; along the alveolar septa the pigment is deposited in irregular masses. By treating sections with a 2 per cent. aqueous solution of ferro-cyanide of potassium, and a one-half of one per cent. solution of hydrochloric acid in glycerin, this pigment remains unchanged, excepting in a few places along the septa, where it alters to a bluish-green color—the characteristic reaction of iron.

Heart: A well-marked segmentation of the heart muscle, with no diastasis and a slight increase in the connective tissue, is noted. A uniform and general deposition of yellowish pigment, which appears as small granules in the myocardial cells. The pigment resembles that of brown atrophy, but gives the microchemical reaction of iron. In certain areas of the specimen some of the nuclei of the myocardial cells are greatly enlarged.

Spleen: The capsule is thickened, with a decided increase in the connective tissue of the organ. The pulp is engorged with blood. There is a small amount of pigment, mostly in the Malpighian corpuscles, and most of the pigment gives the iron reaction, but a little of it shows no change.

Liver: The capsule is greatly thickened; in the substance of the capsule are areas of extensive round-celled

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infiltration and embryonal blood vessels at the outer edge of the capsule, throughout which are brownish-yellow deposits of pigment. Extending from capsule into the parenchyma are heavy bands of connective tissue. These bands encroach upon the liver lobules, in many cases separating them into single lobules or into groups of two or three lobules. This interlobular connective tissue is so increased that in many places the lobules contain but eight or ten hepatic cells. In this hyperplastic tissue are numerous newly-formed bile ducts and some embryonal blood vessels. Throughout the sections, in the interlobular tissue, are numerous areas of leucocytic infiltration. There is quite a marked degree of fatty infiltration, mostly in the periphery of the lobules. There is also seen in the parenchyma a few areas of necrosis, in which the cells are broken up and stain as débris. Throughout the section is a deep brownish-yellow, granular pigmentation. This pigment is deposited in the hepatic cells in the form of regular finely granular masses, which vary in size from one-half to three times the size of a hepatic cell. In many of the cells the nuclei are obscured by this deposit. In the interlobular connective tissue the pigment appears in heavy irregular masses. It is also deposited in the walls of the blood vessels and bile ducts. All of the pigment gives the microscopical reaction of iron.

Kidney: There is a slight increase in the connective tissue; the glomeruli are shrunken and displaced; the cells lining the convoluted tubules appear slightly granular, and the nuclei stain faintly, showing beginning degeneration. The capillaries are distended with blood. The cortical portion contains pigment deposited at intervals in the cells of the convoluted tubules. All of the pigment gives the iron reaction.

Pancreas: The connective tissue is increased throughout the specimen; heavy deposits of pigment are seen; it is observed in the pancreatic cells, but heavier depos-

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its are seen in the connective tissue; all this pigment gives the reaction for iron. There is some round-celled infiltration in the connective tissue. There is a moderate amount of fat throughout the specimen, mostly in the connective tissue.

Bronzed diabetes is a disease characterized by the symptoms of diabetes mellitus to which has been added a general pigmentation, hypertrophic cirrhosis of the liver and usually of the pancreas. Bronzing of the skin is usually present, but not in all of the cases. All of the internal organs are more or less pigmented, the liver containing the largest quantity, then pancreas, heart, spleen, kidney and lungs, the last containing the smallest amount. This pigment gives largely the iron reaction.

In 1871 Troisier observed a case of diabetes in which there was bronzing of the skin; but it was not until 1882 when Hanot and Chauffard in their report of two cases minutely described the disease, both the clinical symptoms and the anatomical findings. Up to the present time there are something like twenty-five recorded cases. All of these have occurred in men and in late adult life. Seventeen of the twenty-five have occurred in France. The disease is unknown in this country, except for one clinical case reported by Berg, in which he bases his diagnosis on the following: "A woman aged 45 had suffered for several years from exophthalmic goiter and the subjective symptoms of diabetes; when she came under observation she had all the symptoms of a severe sugar diabetes, a bronze discoloration of the skin, a slight hypertrophic cirrhosis of the liver, and ascites." The case is rare, being complicated with Basedow's disease and occurring in a woman.

In 1889 Von Recklinghausen reported a number of cases of general pigmentation without diabetic symptoms, and named the condition hemachromatosis. In this country Opie and Adami each reported a case, and

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Osler gives a clinical report of two cases. Writers upon the disease disagree as to its etiology and pathology.

Regarding the etiology of bronze diabetes three theories may be mentioned: 1, that bronzed diabetes is a distinct pathological entity—advanced by Marie and supported by Hanot and other French writers; 2, that it is a diabetes mellitus, the diabetic poisons producing the hemachromatosis, cirrhosis of the liver, pancreas, etc.—advanced by Letulle; 3, that hemachromatosis is the primary affection, and the deposition of pigment causes the hypertrophic cirrhosis of the liver and pancreas, diabetes resulting when the pancreatitis reaches a certain stage—advanced by Opie.

All authorities agree that the pigment which is deposited throughout the different organs and tissues is largely an iron-containing pigment, but the manner in which this is deposited is still a matter of conjecture.

Hanot, Chauffard and Schochman maintain that the changes in the blood are due to the diabetic poisons, causing an abnormal condition of the hepatic cells, whereby the cell metabolism is altered and a deposition of pigment within the cells takes place. The excess is reabsorbed by the blood vessels and lymphatics and deposited in different localities throughout the body in the form of minute emboli.

Letulle, Rendu, De Massory and Hayem believe that pigment is formed in the cell from the hemoglobin of the blood. Hermandez thinks that a dissolution of the blood takes place, and the pigment is deposited in different parts of the body.

Destruction of corpuscles in pernicious anemia, malaria, etc., gives rise to deposit of pigment, but it differs from the pigment formed in hemachromatosis. Welch suggests that the pigment formed in hemachromatosis may be due to a specific form of destruction of the red blood corpuscles.

Adami found in a very large proportion of the pig-

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ment of hemachromatosis distinct diplococci, and comes to the conclusion that the pigment is of bacterial origin, but this has not yet been confirmed by other workers.

January 8, 1900.

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Adami: On Latent Infection and Subinfection, and on the Etiology of Hemachromatosis and Pernicious Anemia. Journal of the American Medical Association, Dec. 23, 1899.

WELLER VAN HOOK demonstrated a carcinoma of the stomach.

November 13, 1899.

WELLER VAN HOOK presented specimens of an old intussusception of the ileum and colon.

November 13, 1899.

WELLER VAN HOOK demonstrated specimens of experimental intestinal obstruction in a dog, produced by wire rings.

November 13, 1899.

WELLER VAN HOOK demonstrated a vermiform appendix eight inches in length.

November 13, 1899.

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THE GENITO-URINARY SYSTEM.

THE PATHOLOGY AND BACTERIOLOGY OF URETERO-INTESTINAL ANASTOMOSIS.

F. ROBERT ZEIT.

Uretero-intestinal anastomosis, or the implantation of both ureters into the rectum, would be a very acceptable procedure to the surgeon in all cases of malignant disease of the bladder, or its neighboring organs, in which the bladder must be removed. Maydl's operation, by which the vesical trigonum with its natural ureteral orifices is implanted into the sigmoid flexure, is only applicable to cases of exstrophy of the bladder. Surgeons have for years experimented to produce uretero-intestinal anastomosis with a view of preventing the bad effects attendant upon the lack of the natural orifices, which allows an entrance of the bacteria of the intestine into the ureters and resulting ascending renal infection and pyelonephritis.

The cases upon which this report is based include the various operations recommended and done by Dr. Franklin H. Martin and Dr. Reuben Peterson on 141 dogs, with a view of devising an operation which should do away with the attendant dangers of such operations, and an experimental study of the pathology and bacteriology of the same. I am indebted to the above-named gentlemen for assigning the latter part of this investigation to me.

After more than two years of faithful work in this direction. I am forced to the conviction that, no matter what operation is done, the pathology of ureteral im-

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plantation into the rectum is the pathology of pyelonephritis and its sequelæ, if it is permissible to judge from operative results upon dogs. It does not appear from the literature that the conditions for recovery in the human individual are much more favorable with better care and control of the patient and better hygienic surroundings.

The high mortality of ureteral implantation into the rectum, 84 per cent., during the first two days even, is a serious objection, but a more important one yet is the fact that dogs which had recovered from the operation and the resulting pyelonephritis, and were to all appearances in perfect health and vigor again, all had granular contracted kidneys. Without exception they all had pyelonephritis shortly after the operation. When killed, from five to thirteen months later, these "cured dogs" were found to have small, hard, contracted kidneys due to induration and cicatrization of the diseased areas following pyelonephritis.

HISTORY.

The extensive literature on ureteral implantation has been collected from original sources in a most thorough manner by Dr. Reuben Peterson[1] and Dr. Franklin H. Martin.[2]

Ureteral Implantation into the Rectum in Dogs.—Of sixty unilateral and sixty-eight bilateral implantations on dogs reported in the literature, with a mortality of 61 per cent. for the unilateral and 85 per cent. for the bilateral operation, the cause of death is given as—peritonitis in fifty-one, stenosis of the ureteral orifice and hydronephrosis in thirteen, pyelonephritis in twenty-nine, and uremia in six. Unfortunately, very few of the experimenters have deemed it necessary to report the pathological or bacteriological findings.

Of the dogs which recovered, not one has been proved to have had healthy kidneys when killed.

Bardenheur,[3] Navaro,[4] Roscizewski,[5] Giordano,[6]

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Weller Van Hook,[7] and Duval and Tesson[8] report that the dogs which recovered from the operation had pyelonephritis, hydronephrosis with hydro-ureter, and stenosis of the ureteral orifice. Kalabin[9] reports one dog with unilateral implantation of the ureter into the rectum as having interstitial nephritis of the corresponding kidney.

Morestin,[10] after ten bilateral and fourteen unilateral implantations, with fatal results in all, concludes

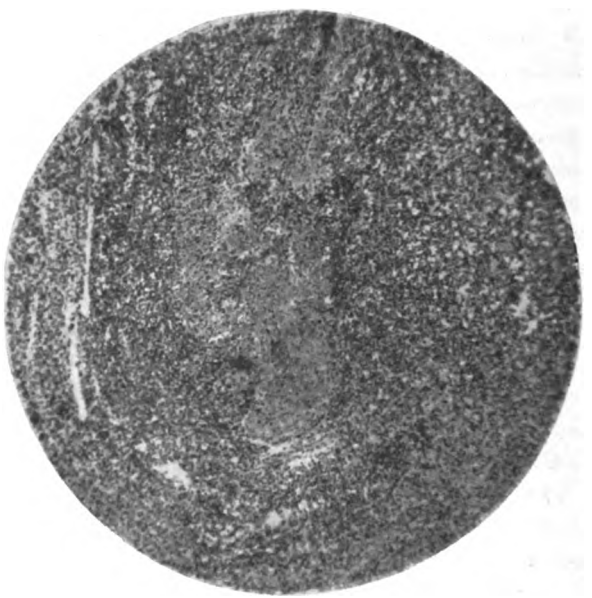

Fig. 1.—Specimen from medullary pyramid. Central necrotic area with colon bacilli in collecting tubules, surrounded by a dense zone of leucocytic infiltration.

that the primary mortality in man should be less than in animals, because of the larger size of the ureters and the possibility of better asepsis.

Giordano,[6] after having done sixteen operations, concludes that without obstruction of the ureters no infection of the kidney should occur.

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Weller Van Hook[7] did ten unilateral and six bilateral operations. His cases were thoroughly examined pathologically and bacteriologically. All the dogs which recovered from the operation—7—had pyelonephritis. He concludes that implantation of one or both ureters into the rectum is an unjustifiable operation under all circumstances.

Chaput,[11] after a series of experiments on dogs with fatal results in all, concludes that experiments on dogs are of but little value as to man, because the bac-

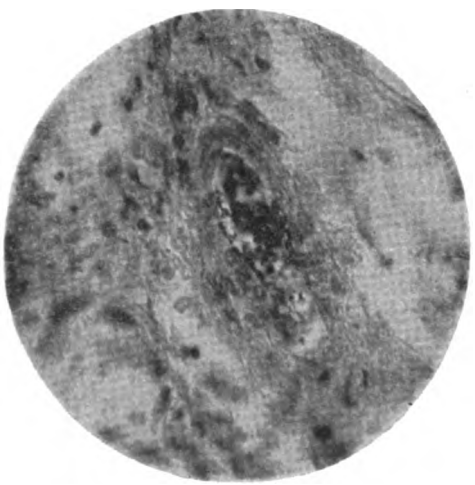

Fig. 2.– Colon bacilli in the blood-vessels.

terial contents of the dog's intestine are more virulent. He fails to bring forward any proof of this assertion.

Frank[12] does not expect any better results in man than in animal experiments.

Ureteral Implantation into the Rectum in Man.— Ureteral implantation into the rectum in the human being was first employed by Simon[13] in 1851. In this case the patient died of pyelonephritis one year after a bilateral operation.

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Smith[14] reports a bilateral implantation with death after fourteen months of pyelonephritis.

Duplay[15] reports two fatal cases of bilateral implantation. Pyelonephritis took place, with death a few months after operation.

Casati[16] had a death from pyelonephritis in thirty-five days after a unilateral operation.

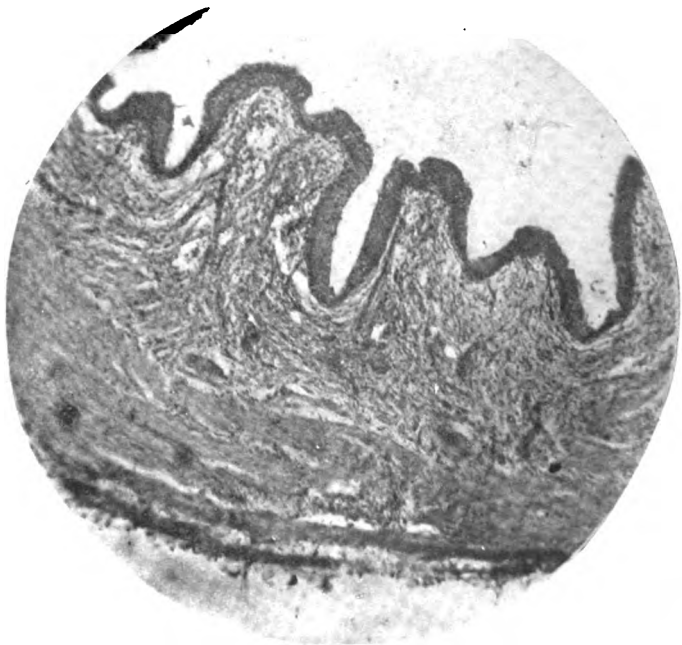

Fig. 3.—Ureter implanted into the rectum. The ureter is comparatively healthy, in strong contrast to the necrotic papillæ and severe pyelonephritis of the same kidney.

Tuffier,[17] Fritsch,[18] Krause,[19] and Wood[20] report similar cases.

Peterson[1] collected thirty-one cases from the literature (seventeen bilateral and fourteen unilateral). Only nine of the patients recovered (five from the bilateral and four from the unilateral operation), a mortality in man of seventy-one per cent.

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If we exclude the four cases of unilateral implantation because the corresponding kidney may have been diseased or inactive, and the patient lived upon his other kidney, there are only five recoveries reported, as follows:

Krause,[19] three months and a half.

Peters,[21] ten months.

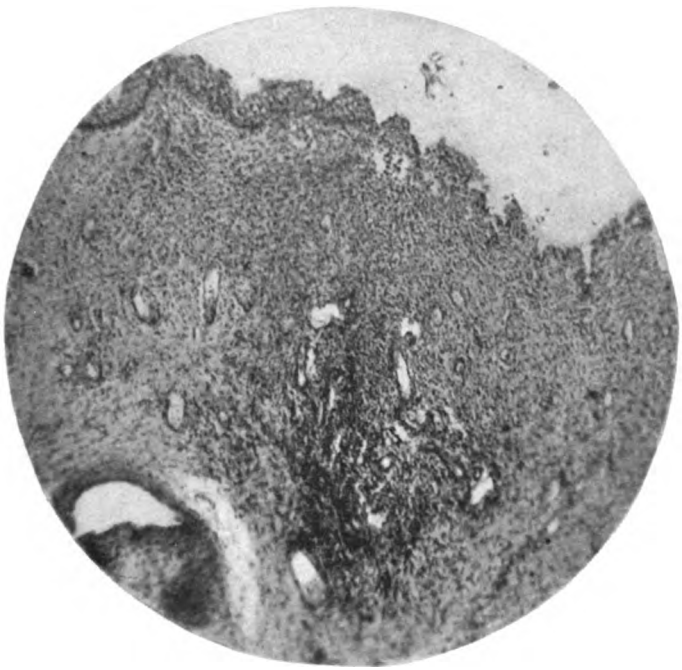

Fig. 4.—Purulent cystitis. The bladders of all dogs with ureters in the rectum are infected by way of the urethra. Small-cell infiltration of the mucosa. Desquamation of covering epithelium.

Chalot.[22] twelve months.

Beck,[23] twenty months. (In this case the patient died in December, 1900, of pyelonephritis.)

Fowler,[24] four years and a half.

The first four can hardly be said yet to be fully recovered, as we shall see presently. This leaves only

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Fowler's case, in which he did a bilateral ureterorectal anastomosis for exstrophy of the bladder in a boy of six years. This patient is still alive, four years and a half after the operation.

Martin[2] concludes that animal experiments will never solve the problem of ureterorectal anastomosis because:

Fig. 5.—Showing the invasion of uriniferous tubules by colon bacilli during the first forty-eight hours after implantation of the ureters into the rectum. The dark portions are bacterial casts in convoluted tubules.

(*a*) The care and hygienic surroundings of the animal can not be so complete as in man;

(*b*) Gravity, exerted upon the urine of the upright human patient, is lacking in the horizontal animal, thus increasing the danger of infection:

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(*c*) The rectum of the human patient can be kept clean;

(*d*) Ureteral catheters can drain the ureters for several days after the operation and thus protect the mouths of the ureters from infection when resistance of the tissues is at its lowest;

(*e*) Compensatory resistance to infection is higher in man.

He thinks the evidence furnished by recorded cases of this operation in the human being "has in it not a little which will stagger the pure theorists."

I have carefully examined his tabulated list of seventy-four cases collected from the literature which he offers as "furnishing the evidence with which to refute the theory of ascending infection in man," and fail to find any material difference in the result from those furnished by his own experiments and those of Peterson on animals. On the contrary, I have been amazed to find in a study of the literature on the subject during recent months how closely the results of my work on Martin's and Peterson's dogs agreed with those in the human being.

We must naturally exclude from Martin's list of the literature of seventy-four cases in the human being all those in which a Maydl operation was done, to make fair comparisons between animal experiments and the results of his operations on dogs. Only cases of ureterointestinal anastomosis should be considered.

Chaput's[11] case, in which the patient is well eight years after implantation of but one ureter, furnishes no proof. The patient is living by his other kidney, as several of our dogs did in which a unilateral implantation was done.

Peters's[21] and Krause's[19] cases, in which the patients were well, respectively, five weeks and three months after the operation, can hardly be considered yet as recovered.

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Chalot[22] and Kryuski[25] report one case in which the patient was well after one year.

Bergenheur[26] reports one patient well after a year and a half.

It is very probable that these patients have the same contracted kidneys which our "cured" dogs showed when killed, after having apparently perfectly recovered from the operation done—300 to 405 days before.

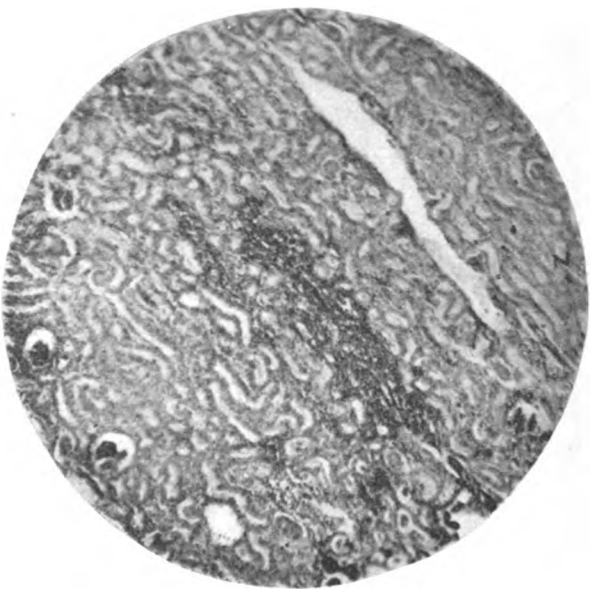

Fig. 6.—Beginning ascending infection within forty-eight hours after implantation of the ureters into the rectum. Hyperemia, marked leucocytic infiltration, and some cloudy swelling.

This leaves only von Eiselberg's[45] two cases, in which the patients were well after three and four years. and Fowler's[24] patient, well four years and a half after the operation, whose case has already been quoted.

Martin's operative results on the human being, which he reported in the same article,[2] also agree with those of his animal experiments. With all his technical skill, acquired by such a large experience in uretero-intestinal

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anastomosis in animals, his results in the human being are not better than those obtained in animals.

It would seem from all this that we can not expect any better results in man than in animal experiments.

Implantation of the Trigonum (Maydl[27]) *for Exstrophy of the Bladder.*—To prevent renal infection, Maydl, in 1894, recommended as an operation for exstrophy of the bladder the implantation of the vesical

Fig. 7.—Thrombosis of the portal vein in a dog that died, thirty days after ureteral implantation into the rectum, from pyelonephritis.

trigonum and its ureteral orifices into the sigmoid flexure. The thirty-six cases collected by Peterson from the literature showed a primary mortality in this operation of 19 per cent. The subsequent results are as follows: After one year, nineteen living; after two years, ten living; after three years, seven living; after four years, four living; after six years, one living; after seven years, one living.

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Pathological and Bacteriological Findings.—Individual reports of some of the findings have already been published, together with descriptions of operations performed by Martin[43] [44] and Peterson.[1] A summarization of them represents a description of the various stages of pyelonephritis and its sequelæ. All the variations of this form of suppurative nephritis have been seen in the dogs operated on—from the earliest beginning of this ascending infection, a few days after the operation, up to the healed condition with induration and cicatrization, the granular, contracted kidneys which are found in all dogs that have recovered from the primary results of their pyelonephritis. The majority of our cases plainly showed that infection could only have taken place by way of the ureters, the pelvis of the kidney, and the uriniferous tubules, and that the pyelonephritis was caused by the bacillus coli communis.

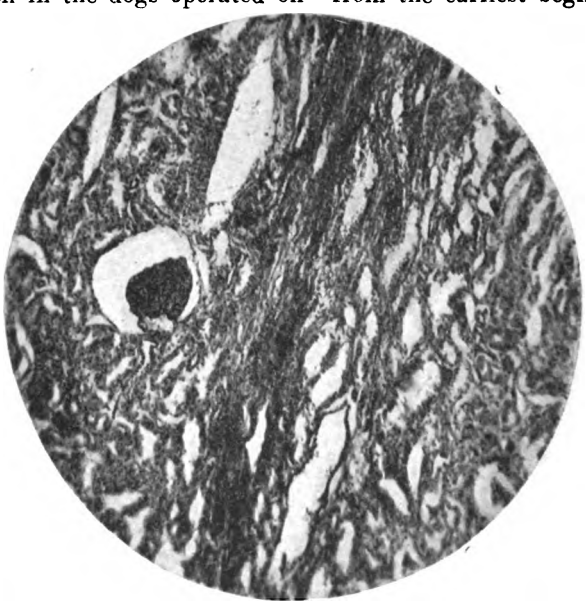

Fig. 8.—Interstitial small-cell infiltration. Dilated uriniferous tubules and capsules. Partly denucleated epithelium.

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The earliest changes are found in the papillæ. Extensive necrosis is seen here very early. Soon after, yellowish flame-like rays extend into the pyramids, and finally small abscesses in the form of yellow elevated granules of the size of a pin head; some with and others without a narrow red zone are seen upon the surface of the cortex. Upon section, these can be seen to extend into the medulla. The kidney is enlarged and soft.

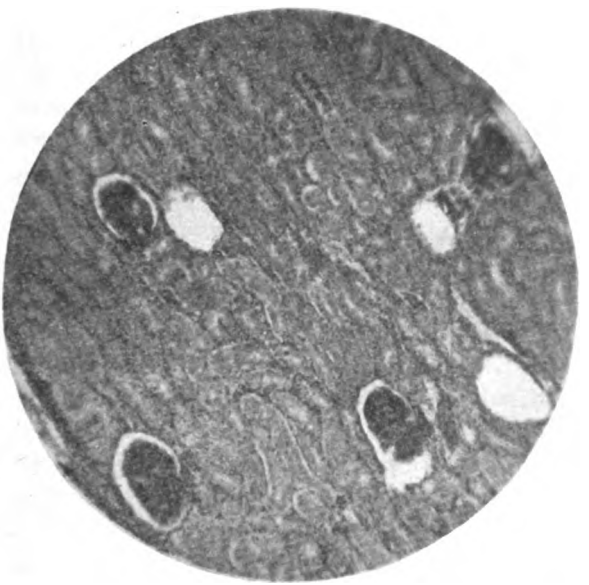

Fig. 9.—Implantation of both ureters into the rectum. The dog died, sixty days after the operation, of pyelonephritis of one kidney. Cloudy swelling and necrosis of the epithelium of the convoluted tubules.

Sometimes only one or more papillæ and medullary pyramids are involved, and their corresponding area of cortex. If the whole kidney is involved, multiple secondary pyemic abscesses and endocarditis lead to the death of the animal. Colon bacilli are found in the lumen of the uriniferous tubules, surrounded by a necrotic and fatty zone, outside of which is a zone of leu-

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cocytic infiltration (Fig. 1). The interstitial tissues and lumen of the tubules contain enormous numbers of polymorphonuclear leucocytes and extravasations of blood, so severe at times that the structure of the kidney becomes obliterated. In the cortex, fatty degeneration and necrosis of the lining epithelium of the convoluted tubules are found in the neighborhood of the affected regions.

Most of the dogs died of peritonitis due to leakage of urine, or general sepsis and pyelonephritis, during the first ten days. Dogs living a longer time died of pyelonephritis, pyelonephrosis, and pyemia, or recovered from the pyelonephritis with contracted kidneys. It was not always easy to determine what form of suppurative nephritis was present. A number of the kidney specimens looked more like embolic suppurative nephritis and infection of hematogenous origin. Pyemia and endocarditis were found in some of these cases, and it became questionable whether they had caused an embolic suppurative descending nephritis, or whether an ascending infection or pyelonephritis had caused the pyemia. It is possible that in some of the cases a blood infection may have been ingrafted secondarily upon an already existing pyelonephritis, because I found colon bacilli in the blood vessels of some of the sections (Figs. 2 and 3).

Orth[28] describes such cases with many small abscesses, distributed over the whole surface of the organ, as having been caused by the entrance of colon bacilli into the arteries, which then produce infectious capillary emboli in the cortex. Aschoff and Gaylord[29] also state that, when large abscesses have formed, the bacteria, having caused the ascending infection, may enter the blood-vessels of the kidney or enter the general circulation by the lymph-vessels, and thus add a descending to the ascending suppurative nephritis. The distinction is usually made that cocci cause the descending embolic suppurative nephritis, and bacilli (coli and

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proteus) the ascending infection, or pyelonephritis, and that in the descending type the bacteria of the small cortical abscesses are in the capillaries of the glomeruli, whereas in the ascending infection they are in the convoluted tubules, having passed up into the cortex from the collecting tubules.

I can not pass this without a brief discussion of the subject of the excretion of bacteria by the kidney. It would seem from our experiments, in which many cases with blood infections occurred, that we should have seen more of the descending infection, or embolic suppurative nephritis; but such was not the case. Several dogs in which only one ureter had been implanted into the rectum died of the pyelonephritis and pyemia, but had only slight or no parenchymatous changes with colon bacilli in the other kidney and in the blood. There can be but one explanation of this observation: Bacteria in the blood are excreted by the kidneys and may pass through normal glomeruli without necessarily producing any anatomical lesions.

With regard to the excretion of bacteria by the kidneys, two essentially different views were held until recently. One is that anatomical lesions must be present in the kidneys to allow a passage of bacteria from the blood into the urine; the other, that the kidney furnishes a perfect physiological filter for all foreign elements of the blood. The first opinion found its greatest defender in Wyssokowitsch,[30] who found staphylococci in the urine six hours and three-quarters after intravenous injection, anthrax bacilli in twenty hours, and streptococci in forty-eight hours, always accompanied by anatomical lesions and rhexis. He found weighty defenders of his views in his teacher, Flügge, and in Birch-Hirschfeld. Extensive experiments by Boccardi,[31] Pernice and Scagliosi.[32] and Konjajeff[33] appeared to support Wyssokowitsch's[30] opinion.

With regard to the second view, which is the gen-

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erally accepted one to-day, that a physiological excretion of bacteria by the kidneys may take place without anatomical lesions, we find that as early as in 1870 Grawitz[34] found hyphomycetes spores in the urine for twenty-four hours without any red blood corpuscles, after intravenous injection. No anatomical lesions were found.

Fütterer[35] [36] described the glomerular excretion of tubercle bacilli in 1885, and typhoid bacilli in the urine

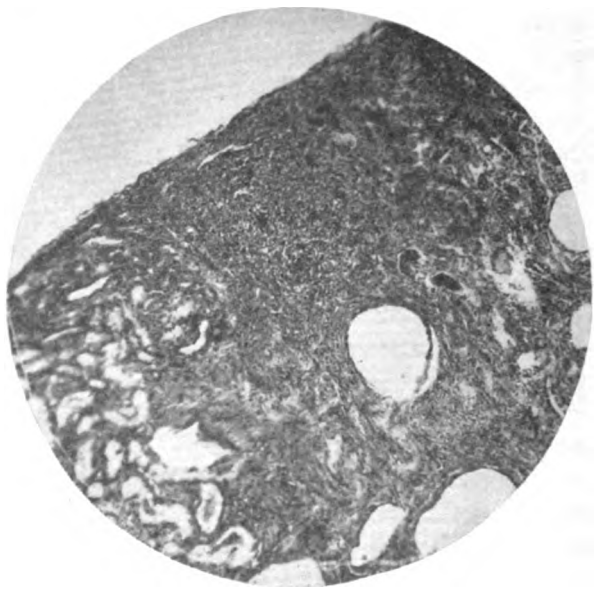

Fig. 10.— Implantation of both ureters into the rectum. The dog was killed ninety days after the operation. Atrophic granular kidney. Much interstitial hyperplasia with contraction and small-cell infiltration. Dilated, desquamated tubules and atrophic glomeruli, with thickened capsules.

in 1888. Fütterer concluded that tubercle bacilli were excreted by the normal kidney without causing tuberculosis of this organ, because his observations on a very extensive postmortem material had shown him that in cases in which the other organs were densely covered with miliary tubercles, only few tubercles were found

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in the kidneys. He argues that in miliary tuberculosis, when the dissemination of the tubercle bacilli takes place, the kidneys must receive a good share of them, and certainly not less than other organs, and we could reasonably expect the kidney to be covered with as large a number of the miliary tubercles as we find in other organs. This can only be explained by the excretion of large numbers of tubercle bacilli by the glomeruli without causing any characteristic lesions.

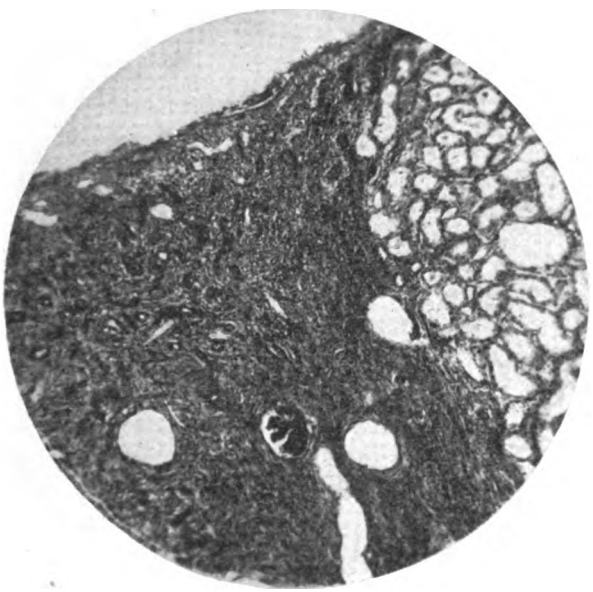

Fig. 11.—See Fig. 10.

Fütterer also instigated Schweizer's[37] experiments, which proved that living and dead foreign bodies might be excreted by healthy kidneys. Fine granules of carmin, barium, and stibium were found in the Malpighian bodies and convoluted tubules, and bacteria in the urine, three hours and a half after intravenous injection. without histologic changes.

Ribbert[38] found staphylococci in the urine six hours

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after injection, without pathologic conditions in the kidney.

Baumgarten's[39] and Ernst Meyer's[40] experiments proved that tubercle bacilli could penetrate normal vessel walls (glomeruli) and enter the surrounding tissue.

Orth[28] states that bacteria may pass the glomeruli in pyemia and produce bacterial casts in the uniniferous tubules, with the cortex and glomeruli remaining normal.

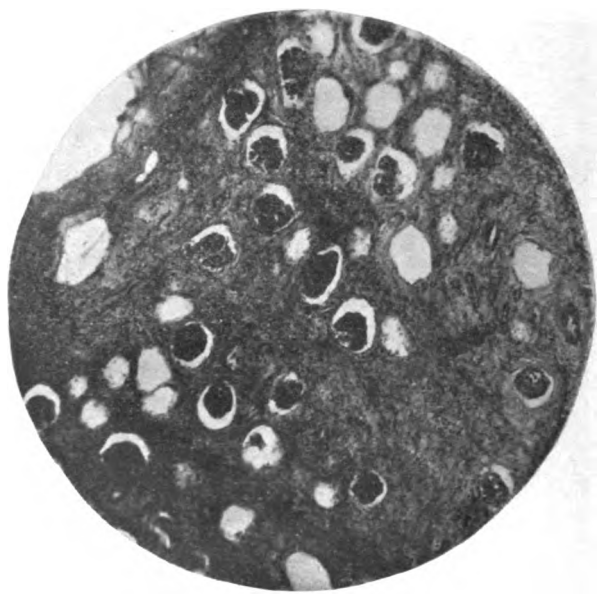

Fig. 12.—Ureteral implantation of both ureters into the rectum. The dog died three hundred days after the operation. Extensive induration and cicatrization. The newly formed and indurated fibrous tissue contains only a few atrophic glomeruli. Here and there small-cell infiltration is present in this scar-tissue.

Biedl and Kraus[41] obtained cultures of the bacillus coli communis, bacillus anthracis, and staphylococcus aureus in ten minutes after intravenous injection from the urine.

Fütterer's[42] experiments of last year, in which he obtained cultures of bacillus prodigiosus from the

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urine two and three minutes after intravenous injection, show that an excretion of bacteria takes place in such a short time that anatomical lesions, such as rupture of vessels and degenerative changes, can be excluded, and that a perfectly intact kidney may excrete bacteria by physiological function without anatomical lesions.

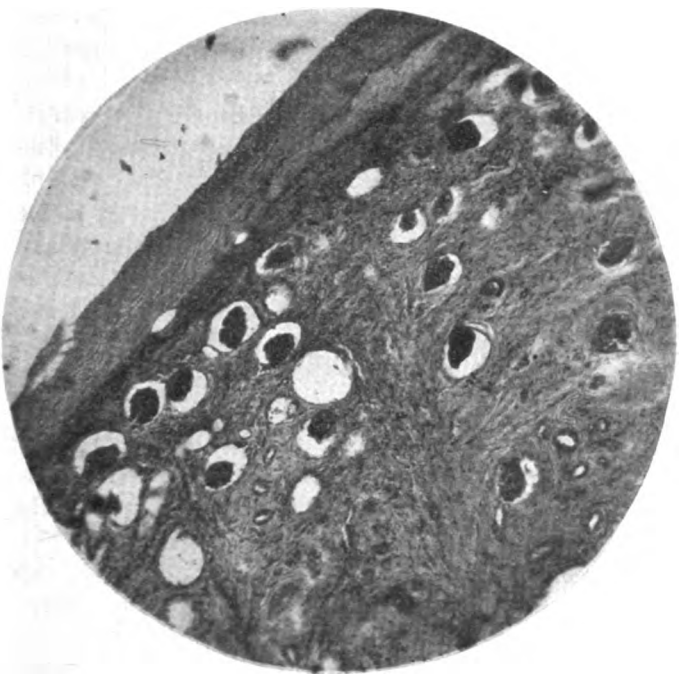

Fig. 13.—See Fig. 12.

Fütterer and I recently undertook some experiments on dogs which go to prove the correctness of this position. Dogs with one ureter tied were injected, by way of the external jugular vein, with 2 cubic centimeters of a twenty-four-hour virulent culture of bacillus coli communis in bouillon, and invariably were found to have pyelonephritis of the ligated side when killed,

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whereas the other kidney remained normal. Control animals had colon bacilli in the bladder for a few days, but both kidneys were found perfectly normal when the animals were killed.

The results following the various operations performed are so uniform that I abstain from describing the operation done. The ureters remain almost normal, although distended at times, and show very little or no leucocytic infiltration, no matter how extensive a pyelitis or pyelonephritis may be present.

After a search of the literature, I believe that Orth's[28] explanation of this phenomenon is the most feasible one.

The motility of colon bacilli is not such that we might expect them to wander up the ureter. They simply rise to the highest level of the stagnant urine, due to more or less stenosis at the opening into the bowel, and thus enter the pelvis of the kidney and multiply there and in the collecting tubules.

Purulent Cystitis.—The bladder was always found to be infected by way of the urethra. In all cases in which the bladder had not been removed it was found to contain a purulent fluid teeming with bacteria, mostly *staphylococcus albus* and *bacillus coli communis.*

Sections show small-cell infiltration of the mucosa and submucosa, with desquamation of the covering epithelium. Peterson thought this effect was produced by not emptying the bladder of urine at the time of operation. I found, however, the same condition present in all the following cases, in which I took the precaution to squeeze out the bladder thoroughly before closing up the abdomen.

The examination of the dogs operated on includes:

1. Anatomical diagnosis.

2. Cultures from (*a*) cortex of kidneys; (*b*) pelvis of kidneys; (*c*) ureters; (*d*) bladder; (*e*) spleen; (*f*) liver; (*g*) heart blood.

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3. Direct cover-glass smear preparations from the same organs.

4. Sections of (*a*) kidneys; (*b*) ureters; (*c*) bladder; (*d*) spleen; (*e*) liver; hardened in alcohol, imbedded in paraffin, and examined for (*a*) bacteria in tissues; (*b*) histopathology.

5. Intraperitoneal inoculation of guinea-pigs with pure cultures of bacillus coli communis obtained by plating out from kidney cortex in eight cases. All the animals died in from twelve to seventy-two hours.

Five dogs which had apparently recovered from the operation were chloroformed and cultures taken, as well as cover-glass smears, from the organs while the animals were alive. Sections of the various organs were placed at the temperature of life in absolute alcohol. This should exclude any possible questions of bacterial invasion of organs soon after death. These five animals were killed: Two dogs forty days after the operation, one dog after ninety days, one dog after 210 days, and one dog 405 days after operation, and all showed recent or old pyelonephritis, as will be seen from the report following.

Ureteral implantation into the rectum was done on 120 dogs (Martin, 76; Peterson, 44), of which number 101 died during the first forty-eight hours after the operation, of peritonitis, due to leakage of urine into the peritoneal cavity, or of general sepsis. I found colon bacilli in the kidney cortex of two dogs (iv P. and 1072 P.), which died within two days after the operation, and in such enormous numbers that the convoluted tubules were packed with them.

Sections showed severe hyperemia, marked leucocytic infiltration and some parenchymatous change. Cultures from the blood and various organs showed a rich growth of bacterium coli commune. Mortality, 84 per cent.

Four dogs died between the second and tenth days

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(P. 805 and 940, P. ii and P. ix), of pyelonephritis and general sepsis.

Dog "A."—Implantation of the left ureter into the rectum. The dog lived eight days (xiii P.). Pyelitis and pyelonephritis of the side operated on. Fibrinous thrombi in both ventricles of the heart, extending into the pulmonary artery and aorta. Colon bacilli in both kidneys and in the blood.

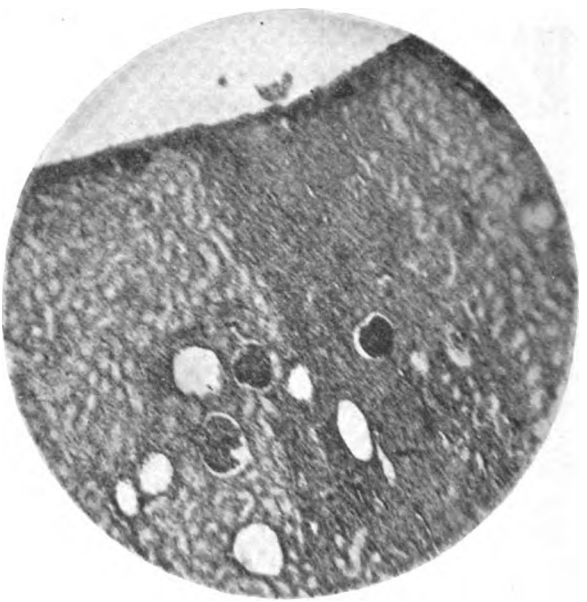

Fig. 14.—Implantation of both ureters into the rectum. Dog killed four hundred and five days after the operation. The elevated portions of the cortex consist of fairly normal parenchyma. Some cloudy swelling is present. The retracted areas consist of newly formed cicatrized connective tissue, with atrophic glomeruli, dilated capsules and leucocytic infiltration of newly formed connective tissue.

Dog "B" lived nine days (ix P.). Pyelitis and pyelonephritis. Extensive medullary changes, necrotic black papillæ.

Histopathology: Many small cortical abscesses with colon bacilli. Necrotic papillæ and colon bacilli in the

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collecting tubules, surrounded by a necrotic area, much leucocytic infiltration, with many polymorphonuclear leucocytes and red blood corpuscles in the interstitial tissue.

Three died on the tenth day, of pyelonephritis and general septicemia (5 and 6 M., iii P.). Pyelitis, pyelonephritis, fibrinous thrombi in the ventricles of the heart; septic spleen. Colon bacilli in the kidney cortex, blood, and spleen.

One died on the thirtieth day, of pyelitis, pyelo-

Fig. 15.—Pyelonephritis thirteen days after implantation of the ureters into the rectum. Many small abscesses in the cortex; the leucocytic infiltration is so extensive that very little of the kidney structure can be seen. Hemorrhagic extravasation and polymorphonuclear leucocytes in the lumen of tubules and interstitial tissues. Colon bacilli in the collecting tubules. Necrotic papillæ.

nephritis (interstitial small-cell infiltration, dilated uriniferous tubules, capsules partly denuded of epilthelium). Thrombosis of the portal vein. Colon bacilli in the kidney cortex and pelvis.

One died thirty-nine days after the operation (iv P., 1128), of pyelonephrosis and pyemia. Endocarditis, septic spleen and liver.

Two dogs were killed forty days after the operation

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(P. i and ii, 1012 and 1032). One (P. i) had small granular atrophic kidneys with distinct evidence of former pyelonephritis. The colon bacilli had been destroyed with the tissue necrosis and cicatrization. The cultures showed no growth.

Histopathology: Proliferation of interstitial connective tissue, forming dense rays from papillæ to cortex, with retraction on the surface of the cortex. Many dilated desquamated tubules. Vessel walls thickened. Some cloudy swelling.

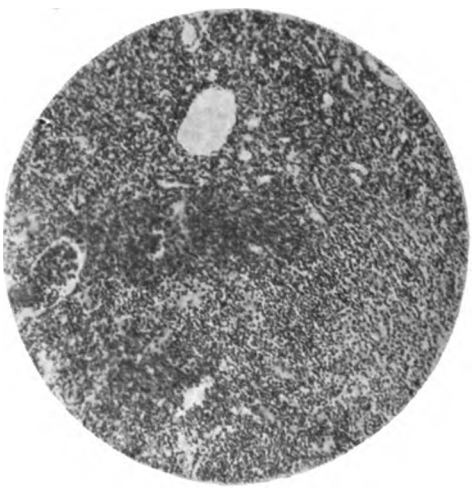

Fig. 16.—See Fig. 15.

The other dog (P. ii) showed pyelitis and pyelonephritis, pyo-ureter, and fibrinous thrombi in both ventricles, extending into the aorta and the pulmonary artery. Pyemia. Cultures show rich growth of colon bacilli from both kidneys, the spleen, the liver, and the blood.

Histopathology: Pyelonephritis.

Macroscopical specimens "C" demonstrated:

One dog died sixty days after the operation (dog 5, P.), from pyelonephritis and pyemia of one kidney and

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parenchymatous nephritis of the other kidney. The right kidney was granular, with millet-seed cortical abscesses containing colon bacilli. Adherent capsule, old and recent pyelonephritis. The left kidney was enlarged and pale, and the capsule stripped off easily. No bacteria were found in smears or culture. Thrombosis of the portal vein, colon bacillus, and staphylococcus infection of the liver. Fibrinous thrombi in the right auricle and ventricle, with staphylococcus albus. Purulent cystitis.

Histopathology: Right Kidney.—Pyelonephritis and granular atrophy. Hyperplastic interstitial connective tissue in the form of rays from papillæ to cortex, with cicatricial retraction of the surface of the cortex. Dilated tubules, with desquamated epithelium and granular detritus. Vessel walls thickened. Some cloudy swelling and necrosis.

Left Kidney.—Parenchymatous nephritis, cloudy swelling, fatty degeneration, and necrosis of epithelium of the convoluted tubules. Very little interstitial change.

Two dogs died eighty-four and eighty-seven days after the operation (dogs 3 and 8, P.). The first (eighty-four days) died of pyelonephrosis and pyemia (mixed infection), pyelonephrosis, and pyo-ureter on the right side. Bacillus coli communis and staphylococcus albus. Pyelonephritis of the left kidney. Fibrinous thrombi in the heart. Septic spleen and liver, with colon bacilli. Purulent cystitis with staphylococcus albus.

The second dog (eighty-seven days) died of pyelonephritis and pyemia (mixed infection). Slightly granular kidney, with adherent capsule and pyelonephritis. Pyo-ureter. Septic endocarditis with fibrinous thrombi. Staphylococcus albus and colon bacilli in the spleen, liver and heart. Colon bacilli in the ureter and kidney.

One dog was killed ninety days after the operation

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(M., 4). Cultures taken from the live organs (chloroform narcosis).

Right Kidney.—Macroscopic specimen "D" demonstrated: Recent pyelonephritis, with colon bacilli. Non-adherent capsule. Millet-seed abscesses over the whole surface of the kidney, purulent rays from papillæ to cortex.

Left Kidney.—Old pyelonephritis, with granular atrophy of the middle of the convex border and adherent capsule. No bacteria.

Purulent cystitis with staphylococcus aureus and colon bacilli, septic spleen and liver (staphylococcus aureus and colon bacilli). Ureters comparatively healthy.

Histopathology: Atrophic granular kidney. Much interstitial hyperplasia with contraction and small-cell infiltration. Dilated, desquamated tubules and atrophic glomeruli with thickened capsules.

One dog died 127 days after the operation (M., 1), of pyelonephritis and pyemia. Pyelonephritis and pyelitis of both kidneys, colon bacilli in both kidneys (uriniferous tubules) and ureters. Thrombosis of the portal vein. Septic spleen. Cystitis. The bladder contained purulent fluid with colon bacilli and staphylococcus albus. Fibrinous thrombi in the heart. Legs edematous, with purulent exudate in the subcutaneous tissues and colon bacilli.

One dog was killed 210 days after the operation (M., 7). Macroscopic specimens "E" demonstrated: Old pyelonephritis with granular atrophy. Hydronephrosis of both kidneys and hydro-ureter. No growth of bacteria in cultures. Purulent cystitis with colon bacilli and staphylococcus albus.

One dog died 300 days after the operation (3, M. 851) with small granular atrophic kidney, the result of old pyelonephritis. No bacteria found.

Histopathology: Extensive induration and cicatri-

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zation. The newly formed and indurated fibrous tissue only contained a few atrophic glomeruli; here and there small-cell infiltration was present in this scar tissue.

One dog was killed 405 days after the operation (P., 10). Macroscopic specimens "F" demonstrated: This dog had perfectly recovered from the operation and was, to all appearances, in the very best of health when we killed him. Cultures and smears from all the organs showed no bacteria present. Both kidneys had opaque adherent capsules, with deeply branching cicatricial retractions of the surface, having macroscopically the appearance of arteriosclerotic contracted kidneys. Both ureters were dilated. Sections of the kidneys showed distinct evidence of an old pyelonephritis. Radiating, yellow, ray-like lines from papillæ to cortex surface.

Histopathology: The elevated portions of the cortex consisted of fairly normal parenchyma. Some cloudy swelling was present. The retracted areas consisted of newly formed cicatrized connective tissue with atrophic glomeruli, dilated capsules, and leucocytic infiltration of newly formed connective tissue. The many small cortical abscesses of pyelonephritis seen in other cases had resulted here in infarct-like retractions by scar tissue.

IMPLANTATION OF THE TRIGONUM INTO THE RECTUM.—Peterson operated on twenty-one dogs, of which number, sixteen died during the first few days (76 per cent.), of peritonitis and general sepsis. He thinks that twelve deaths were clearly due to faulty technique.

One dog died eight days after the operation, from pyelonephritis and pyemia. The left half of the trigonum with denuded mucosa, the right half with mucosa intact, were implanted into the rectum. Pyelitis and pyelonephritis of the left kidney. Hyperemic right kidney, otherwise normal. Fibrinous thrombi in the heart. Abdominal wound sloughing, and pelvic abscess. Colon bacilli in both kidneys, the spleen, and the heart.

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One dog was killed thirteen days after the operation. Macroscopic specimen "G" demonstrated: The dog was much emaciated and dying from pyelonephritis. The right ureter was implanted into rectum by the former method. The left ureter with the trigonum was implanted into the rectum. The results are highly interesting. The right kidney showed a well-marked pyelonephritis with pyelitis, necrotic papillæ, and opaque capsule. The cortex was covered with yellow, purulent, millet-seed abscesses, surrounded by hyperemic zones. Yellow and red flame-like rays from papillæ to cortex. Colon bacilli in smears and cultures. Left kidney, normal. No bacteria.

Histopathology: Fully developed pyelonephritis of the right kidney. Many small abscesses in the cortex. The leucocytic infiltration was so extensive that very little of the kidney structure could be seen. Hemorrhagic extravasation and polymorphonuclear leucocytes in the lumen of the tubules and in the interstitial tissue. Colon bacilli in the collecting tubules. Necrotic papillæ.

Left Kidney.—Hyperemic, with some cloudy swelling of the lining epithelium of the convoluted tubules. No bacteria.

One dog was so sick on the forty-fourth day that we killed him. Macroscopic specimen "H" demonstrated: Pyelonephritis and pyemia. The trigonum with both ureters was implanted into the rectum. Too much ureteral mucosa was removed, implanting flaps transversely across the bowel. Both kidneys showed advanced pyelitis and pyelonephritis and adherent capsules. Pyoureter of the right side. Colon bacilli in both kidneys. Fibrinous thrombi in both ventricles and auricles. Result the same as in uretero-intestinal anastomosis.

One dog was killed on the fifty-ninth day after the operation. Macroscopic specimen demonstrated: Trigonum implanted into the rectum. Ureters slightly di-

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lated. No pyelonephritis. Capsule stripped off easily. Smears and cultures negative.

Histopathology: Parenchymatous nephritis.

One dog was killed sixty-five days after the operation. Macroscopic specimen "K" demonstrated: The left ureter with half of the trigonum implanted into the rectum. This dog was in perfect health, apparently, when killed. Very small, atrophic left kidney. Capsule adherent and surface slightly nodular. Left ureter much dilated and non-patent. No bacteria in smears and cultures. Compensatory hypertrophy of the right kidney. Purulent cystitis.

ANIMAL EXPERIMENTS WITH BACILLUS COLI COMMUNIS.—It has been shown by the preceding reports that an ascending infection by the bacillus coli communis takes place in every case of uretero-intestinal anastomosis, which led me to undertake some experiments with a view to producing an artificial immunity against infection by these organisms. The animals experimented upon were white rats and guinea-pigs.

Virulence of Bacteria.—The virulence of the colon bacillus varies much, according to the different sources from which it is obtained. But even from the same source we cultivated bacteria which were identical in morphological and cultural characteristics, and yet varied greatly in their virulence.

The name of this bacillus stands for a whole group of bacteria. In order to determine the virulence and lethal dose of bacillus coli communis to be used for immunization, I employed pure cultures obtained from two sources. In all cases, twenty-four-hour bouillon cultures were used (second generation), which were inoculated from discrete colonies on agar plates (first generation).

A, 1.—Second generation, from a case of colitis membranacea of Dr. Emil Ries.

(*a*) *Guinea-pigs.*—Intraperitoneal injection of 2 cubic centimeters killed a guinea-pig of 500 grams in eighteen

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hours. Smallest lethal dose, 0.2 cubic centimeter. At the autopsy a hemorrhagic exudate was found in the peritoneal cavity, with colon bacilli and great distension of the large intestine. Colon bacilli in the heart blood, the spleen, and the liver.

(*b*) *White Rats.*—Intraperitoneal injection of 2 cubic centimeters killed a white rat of 180 grams in from twelve to eighteen hours. Autopsy: Great distension of the colon. Hemorrhagic exudate into the peritoneal cavity. Colon bacilli in the exudate, the heart blood, the spleen, and the liver. Smallest lethal dose, 0.4 cubic centimeter.

A, 2.—Second generation, from a case of colitis membranacea of Dr. Emil Ries. Intraperitoneal injection of 2 cubic centimeters. Guinea-pig weighing 380 grams:

		Degrees.		Grams.
2d day:	Temperature,	101.;	weight,	370
3d "	"	101.6;	"	320
4th "	"	102.;	"	310
5th "	"	102.;	"	285
6th "	"	101.4;	"	295
7th "	"	101.;	"	315
8th "	"	101.;	"	333
12th "	"	100.2;	"	360

B, 1.—Second generation, from the rectum of a healthy guinea-pig of 370 grams. The same guinea-pig, inoculated with 2 cubic centimeters, showed loss of weight and lowered temperature for several days, but recovered completely within ten days, at which time its weight was the same as before inoculation.

B, 2.—Second generation from the rectum of a healthy guinea-pig. One cubic centimeter killed a guinea-pig of 350 grams in from twelve to eighteen hours.

It is evident from this that, of the four cultures used, only two (A. 1 and B, 2) were virulent, although no cultural or morphological difference could be made out between virulent and non-virulent cultures.

Immunity.—Löffler and Abel[46] have already shown that the poisonous principle of the colon bacillus is in the

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bacterial bodies and can not be separated, so we used for our experiments:

1. Living cultures of virulent colon bacilli, one-tenth of lethal dose, by subcutaneous injection.

2. Cultures killed by heat.

A white rat of 177 grams was injected subcutaneously with 0.04 cubic centimeter of living culture A, 1.

		Degrees.		Grams.
1st day:	Temperature,	101.;	weight,	170
2d "	"	101.;	"	160
3d "	"	101.;	"	155
4th "	"	100.;	"	160
5th "	"	99.;	"	161
6th "	"	99.;	"	171
8th "	"	99.;	"	172
10th "	"	99.;	"	180

On the twelfth day another subcutaneous injection of 0.08 cubic centimeter was made, without fever reaction or loss of weight.

On the 14th day, 0.1
On the 19th day, 0.2
On the 24th day, 0.4 (Lethal dose.)
On the 30th day, 1.0

A large necrotic area with hard, swollen base and circumference had formed on the abdomen where the injections had been made. This animal now received an intraperitoneal injection of 1 cubic centimeter of this virulent culture—that is, more than double the lethal dose—but without effect. A serum test showed marked and immediate clumping of bacilli in a dilution of one drop of blood with fifty drops of bouillon culture.

When we tried the same reaction with other colon cultures, it proved negative. The animal then received an intraperitoneal injection of 2 cubic centimeters of the virulent bouillon culture B, 2, and died the same night. The autopsy showed hemorrhagic exudate with colon bacilli in the peritoneal cavity and in the heart blood and the spleen. It appears from this that the animal was immune only to bacterium coli, A, 1.

The same experiment was done on several guinea-pigs

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with practically the same results. We now used dead cultures (killed by heat) of the same bacterium coli, A, 1, in a third generation for immunization of another guinea-pig, and found again a positive serum reaction after we bled the animal to death to obtain the serum. This serum clumped only the same colon bacilli which were used to produce the immunity.

The experiments are not concluded, and will be the subject of a future paper; but it would seem from the results obtained so far that artificial immunity to the group of bacilli constituting the so-called colon group, to prevent ascending infection in cases of ureteral implantation into the rectum, is impossible, although it is the only hope of making such an operation feasible.

Implantation of the trigonum into the rectum (Maydl's operation) can not be done in cases of malignant disease of the bladder. The same may be said of vesicorectal anastomosis (Frank).

These operations are very efficient in the prevention of early ascending infection, but, of course, out of the question where the trigonum is diseased and the bladder must be removed.

Renal infection does not take place until very late, when the normal ureteral vesical orifices become deficient and an ascending infection or pyelonephritis may follow in the same manner in which it occurs in an old purulent cystitis. For a time the normal vesical orifices resist the entrance of bacteria, until a purulent cystitis encroaches also upon the region of these valve-like structures, and then pyelonephritis results. Artificial immunity would seem here, also, the only resource.

CONCLUSIONS.

1. Ureteral implantation into the rectum is always followed by ascending infection. The resulting pyelonephritis is caused by the bacillus coli communis.

2. The primary mortality is very large, 84 per cent., no matter which operation is done.

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3. Of 120 dogs operated upon, 90 per cent. died of peritonitis due to leakage of urine or general sepsis and pyelonephritis during the first ten days.

4. Dogs living a longer time died of pyelonephritis, pyelonephrosis, and pyemia.

5. Dogs which had fully recovered from the operation and the resulting pyelonephritis, and were, to all appearances, in perfect health and vigor again, all had granular contracted kidneys, due to induration and cicatrization of diseased areas. The rectum acts as a fair substitute for the bladder in such cases.

6. Dogs which had fully recovered after unilateral implantation were living by the other kidney. The kidney of the side operated on was atrophic and granular, the result of an early pyelonephritis. The functionally active kidney was of two to eight times the size of the atrophic one.

7. A review of the literature on uretero-intestinal anastomosis in man shows that no better results can be expected in man than in animal experiments.

8. The ureters are frequently dilated, but show very little or no disease, no matter how extensive a pyelitis or pyelonephritis is present.

9. The bladder is always infected by way of the urethra, whether it is emptied at the time of operation or not. A purulent cystitis was found in every case, caused by staphylococcus albus and bacillus coli communis.

10. Artificial immunity to infection by the so-called colon group of bacteria is the only hope of making uretero-intestinal anastomosis a feasible operation.

December 10, 1900.

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SPONTANEOUS AMPUTATION OF BOTH FALLOPIAN TUBES.

EMIL RIES.

In September, 1899, Dr. C. T. Murphy kindly asked me to see a case with him which, on account of its extraordinary pathological finding, is well worth recording. The patient was a married woman, 32 years old, whose menstruation had begun at the age of 13 years and had been regular though at times painful. For years she had some leucorrhea. Married at the age of 18 years, she had one child 11 years ago, which is alive and well, and two miscarriages of seven months each, one twelve, one eight years ago. Ever since the first confinement she has been ailing and her menstruation has become scantier and more painful. Four years ago her present trouble began with severe pain in abdomen and back. For a week before I saw her she was confined to her bed with severe abdominal pain, temperature as high as 103, loss of appetite, nausea, inability to move. She was constipated and had some burning pain on urinating. Examining her (September 18) I found a small, thin, pale, poorly nourished woman with a temperature of 99, pulse 100, urine free from albumin and sugar. Heart, lungs, liver, spleen without abnormalities. No enlargement of lymphatic glands. The vulva and vagina contained a little whitish discharge. The vagina was large, its walls smooth. A little pus could be squeezed from the left labial gland, nothing from the urethra or right labial gland. Cervix slightly lacerated to the right and left, uterus in anteversion; on the left side the ovary could be felt, on the right side a plainly fluctuating and very painful sac. A diagnosis of inflammation of the right

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appendages was made and a vaginal operation was recommended.

The operation was performed on September 19 and lasted about thirty minutes. An incision was made around the cervix, the bladder separated from the uterus and peritoneum of the vesico-uterine pouch opened. The uterus was brought down into the vagina and it was seen immediately that the tubes formed only very small stumps on either uterine horn. On the right side the rest of the tube presented itself as a bluish-black sac of the size of a goose egg. The operation was then proceeded with so that the ligament was severed after hemorrhage had been provided against by temporary clamping. In this way the broad ligament of the left side was severed and then the uterus was cut free posteriorly. The uterus was pulled over to the right side. The clamps were removed step by step as a continuous catgut suture starting from the suspensory ligament of the ovary closed the broad ligament. The uterine artery, which was plainly visible, was ligated. Now, the same process of first cutting and clamping and then replacing the clamps by a continuous catgut suture was carried out on the right side. Then the pelvis of the patient presented a row of sutures over the right and left broad ligaments between which the dark sac of the right tube was plainly visible. This sac was in no connection with the uterus or the broad ligaments where they had been cut and sutured, but was held in place by a few thin bands of adhesions with the right lateral pelvic wall, which were torn easily and required only one ligature. Now the peritoneum of the bladder was united to that of the cul-de-sac by a continuous catgut suture. Over this the vagina was closed in the same way by a continuous catgut suture. A dressing of sterile gauze was placed in the vagina.

The patient made a smooth recovery, sat up in bed twenty-four hours after the operation, sat up in chair

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and walked forty-eight hours after the operation,[1] and left the hospital exactly one week after the operation (September 26). Examination at this time showed the fornix healed smoothly, the catgut suture could still be felt at some points. The general condition was excellent, patient was free from pain. I have seen her again about one month after the operation, when she came in a street-car, a distance of about seven miles. Her appearance was splendid, she looked stouter and stronger, was free from all pain, had a good appetite and regular digestion. The vaginal scar was linear and the pelvic condition presented nothing abnormal. I have again examined the patient on December 14. She has gained 13 pounds and is able to work as a sewing-machine teacher, going to the houses of purchasers and instructing them in the use of the machine. Her condition locally as well as generally is highly satisfactory.

The specimen removed by this operation consists of uterus, stumps of both tubes, ovaries and ovarian ligaments, and the right hematosalpinx. The uterus is 6.5 centimeters long, has a good muscular wall, the fundus is well rounded and its top reaches higher up than the starting points of the tubes. The stump of the left tube has a diameter at the base of 5 millimeters, its lengh is above 12 millimeters, below it protrudes only 4 millimeters, its length on top is 17 millimeters, below it protrudes 7 millimeters. The stumps are soft and tapering towards their ends where they terminate in a very small cone without any opening. The peritoneum which covers the stump of the right tube extends from this stump downwards uninterrupted to the ovarian ligament, investing the lateral edge of the uterus between tubal stump and ovarian ligament. On the posterior surface of the uterus extending on to the tubal stump

1. "Some radical changes in the after-treatment of cellotomy cases." JOURNAL A. M. A., August, 1899.

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some remnants of adhesions are found. Adhesions are also found on the part of the ovary near the uterus and on the posterior or rather inner aspect of the ovary. The right ovary contains a good-sized corpus luteum. The left tubal stump shows a very few fine bands of adhesions anteriorly. The peritoneum covering it again invests the edge of the uterus down to the point of insertion of the ovarian ligament. The ovary of this side is of about the same size as the right one and shows a few prominent cysts. Some bands of adhesions are also low down on the posterior surface of the uterus whereas the anterior surface is free from adhesions.

The detached right tubal sac has a length along its upper border of 10 centimeters and a largest circumference of about 9 centimeters. It is somewhat pear-shaped, the outline being irregular in consequence of a number of shallow constrictions. The uterine end forms a small cone completely closed and covered with peritoneum. The abdominal end is rounded and shows a shallow dimple as a remnant of the fimbriated opening. The upper part of the uterine end presents a few thin bands of adhesions, as do also the anterior and posterior surfaces. There are three small cysts, probably hydro-parasalpinx, on the lower surface of the sac. It is important to note that, aside from the adhesions, the cut surface where the tube was in connection with the neighboring tissues is not more than about 10 millimeters long and at its widest point 5 millimeters wide. All the rest of the tubal sac is covered with smooth peritoneum and therefore must have been unattached.

On opening the sac a serous fluid with a bloody tinge escapes and when the tube is cut open along its upper border it is found to present on its inner surface prominent ridges corresponding to the slight constrictions on the outside. The inside of the sac is lined with a blackish mucosa, the surface of which is irregular and somewhat ragged. In the fluid a smooth body is found, of

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irregular shape, without any pigmentation, slightly transparent and very soft. Microscopic examination of this body shows it to consist of threads of fibrin, red and white blood corpuscles. Transverse sections of the wall of the sac show hemorrhagic infiltration of the tubal wall without any signs of inflammatory processes. The muscular wall is thin and the fibers of the wall are separated in many places by masses of red blood corpuscles. This infiltration with blood becomes even more marked in the mucosa, where the epithelium of the surface is lifted away in some spots from the underlying tissue by the masses of blood and is flattened and thinned; at a few points it can not be found at all. Deeper down between the well-pronounced folds of the mucosa the epithelium is cylindrical, normal.

We have here a case of amputation of both tubes and formation of hematosalpinx in the detached abdominal part of the right tube, whereas the left tube is completely lost beyond the small stump.

There are two points in this case which can easily be determined beyond any doubt. The one is that the amputation is spontaneous, as neither the history nor the examination of the patients present the slightest indication of operative interference with the tubes previous to my operation. The second point is that the amputation and occlusion of the tubes is an acquired one, as shown by the three pregnancies which the patient went through, as at least one side must have been patent when the patient conceived.

Beyond these two points, however, there are considerable difficulties in the interpretation of the pathology of the case.

There is, first of all, the difference between the two sides, one side showing no trace of tube beyond the small stump, while the other side presents a tumor of the detached portion of the tube. What has become of the

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missing part of the left tube? The first possibility is that I overlooked it in the operation or that it was so high up that in the vaginal operation it could not be found. The objections against this theory are the following: First, the most careful search revealed no trace of the tube either during the operation or on subsequent bimanual palpation, nor is it likely that the tube could not be found during the operation because of its being located too high up, as an incomplete descensus of the tube is not probable without the ovary being affected in the same way, and the left ovary was found in its normal position in the course of the operation.

If, therefore, we have to assume that the left tube was not found because there was none, we have to consider two further possibilities, one being that the tube did not develop at all—which is not likely, as in non-development of the tube the entire tube is absent without a trace of a stump, and also because the ovary of this side was fully developed, the other one assuming that the tube, after having been developed, was separated from the uterus and the broad ligament by some process and became absorbed. Such a process of separation may have taken place during the intra-uterine or the extra-uterine life. An intra-uterine peritonitis, for instance, may have given rise to pseudo-membranes which separated the tube from the stump and permitted it to become absorbed just as parts of extremities, etc., may become absorbed after strangulation by amniotic bands, and in the same way as young embryos implanted free into the peritoneal cavity become absorbed, as described by Leopold. Another explanation might again be given in an incomplete descensus of the Mullerian duct leading to overstretching of the tube and thereby separation with subsequent absorption. But this is not probable, because, as mentioned above, the ovary had gone through the normal descensus. In extra-uterine life the tube of the left side may have become detached in consequence of peritontic

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adhesions. A few remnants of peritonitic pseudo-membranes are still visible on the tubal stump. Such adhesions have repeatedly been observed to cause amputation of the tube, as, for instance, by Rokitansky and by Klob. In a recent paper by Ruppolt (*Archiv f. Gyn.*, vol. 47) a case is described in which the uterine end of the tube has become separated from the abdominal part of the tube and where the ovary also has been cut in two. In one part of the ovary of Ruppolt's case a dermoid had developed, which had given the indication for the operation. In his case there were adhesions between the omentum and the point where the tube had become separated. He considers his case due to intra-uterine peritonitis, but it is impossible to disprove its causation by peritonitis in extra-uterine life even though the history of the patient does not contain any definite data in this respect.

It is *à priori* very probable that in my case a localized peritonitis had given rise to the amputation of the right tube at the uterine end. The remnants of such a peritonitis are still to be found in the occlusion of the abdominal end of the right tube and in the pseudo-membranes of the posterior wall of the uterus, of the ovary, etc. (see above). Formation of tumors in the ovary and subsequent overstretching of the tube, which partakes in the formation of the pedicle of the ovarian tumor, has repeatedly been observed to produce amputation of the tube. I have observed such a case in an operation for dermoid of the right ovary, where the tube formed only a very short stump, ending in an occluded small cone. But in the case under discussion now there was no tumor of the ovary. It is also possible that in the migration of the tube along with the pregnant uterus the left tube was carried up high into the abdominal cavity, then became adherent, and subsequently, when the uterus retired again into the pelvic cavity, could not follow and was then so overstretched that it gave way near the

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uterus and either still is high up somewhere in the peritoneal cavity or has become absorbed.

If we turn to the right side of the specimen we have, as already mentioned, evidence of peritonitis in the occlusion of the abdominal end of the tube and in adhesions which the specimen shows very plainly. This would favor the theory that the amputation of the uterine end of the tube on the right is also due to these peritonitic membranes. But here another point has to be taken into consideration, the presence of the hematosalpinx on this side. The microscopic examination of the tubal sac shows plainly that we have to deal, not with a hemorrhagic inflammation, but with a hemorrhagic infiltration of the wall of the hydrosalpinx. What caused this hemorrhagic infiltration? In answering this question it will be well to take into account the results of a paper by Praeger (*Arch. f. Gyn.*, vol. 58). In this paper twenty-two cases of tubal tumors are reported, in which torsion of the pedicle of the tubal tumor had taken place. It is clearly demonstrated in this review of Praeger's that in consequence of such torsion of the pedicle hemorrhagic infiltration, sometimes proceeding even to hemorrhagic necrosis, takes place, and also that in consequence of this torsion of the pedicle of the tubal tumor the tube may become so much twisted that an amputation as a consequence is not impossible. In two cases reported by Von Herff and Hirst the tube had become almost completely severed at the point of the twist.

Is it not possible that in our case the right tube became separated in consequence of such torsion of its pedicle? The exceedingly small size of the pedicle of the hematosalpinx, as described above, would certainly favor such torsion of the pedicle. But though such an etiology of the case would stamp it as highly interesting, in fact, as a unique case, I have seen myself obliged to abandon this theory. The symptoms of an acute inflammatory condition in the pelvis of the patient, which she

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had for a short time before I operated, and which usually accompany torsion of the pedicle of a tubal tumor, the condition of the pedicle, the microscopic findings in the tube which show the hematosalpinx to be of recent date, make it necessary to assume that the hemorrhagic infiltration of the tubal wall is of recent origin, whereas the amputated stumps and the occlusion of the abdominal end are plainly of older date. Though I have no doubt but what the patient's right hydrosalpinx had undergone torsion of the pedicle at the time when she was taken sick, I can not believe that the amputation of the tube was also produced by this torsion. I rather believe that in consequence of a peritonitis with formation of pseudo-membranes the right tube as well as the left became amputated, the right tube occluded at its abdominal end, a hydrosalpinx formed with a very small pedicle. This pedicle subsequently became twisted, hematosalpinx formed, giving rise to the acute symptoms, which necessitated operative interference.

As to the operative treatment in this case, it might be questioned whether the radical procedures which I followed were justified or if it would not have beeen better to try conservative methods. Through the ingenuity of our president, Dr. T. J. Watkins, we possess an operation which enables us to join the isthmic portion of the tube with the uterus after the connection between the two has been interrupted, be it by operative interference or as in this case by pathological conditions. A salpingo-hystero-anastomosis could have been performed in this case. I might have opened the abdominal end of the tube, permitting the escape of the contents of the tube, might have cut open the uterine end of the hematosalpinx, might have removed the uterine stump of the tube, incising the uterine horn clear down to the cavity, and might then have inserted the tube into the uterus. But as I had to deal with an infected uterus and with a tube which had been inflamed and about the asepsis of which

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I could not state anything positively at the time of the operation, I preferred radical measures. At any rate, if I had tried to be conservative it would have been necessary to give the right tube a better pedicle than it had, in order to insure its nutrition and to prevent the return of the torsion of the pedicle. Though it is a more pleasant task for the surgeon to return organs damaged by pathological processes to their normal functions rather than to remove them, in this case I did not feel called upon to reconstruct a female sexual apparatus which, by its pathological changes, had become a danger to the woman's health.

December 11, 1899.

ON THE PATHOLOGIC FORMATION OF CORPUS LUTEUM TISSUE.

LEO LOEB.

The following treats of the ovary of a calf, which presented several unusual features. I have not found a similar ovary described in literature.

The ovary was that of a calf six months old. The animal had suffered from actinomycosis of the face, and for that reason had been killed. The postmortem examination (at which Dr. Jobson was present) showed all the other parts free from actinomycosis. The uterus was not enlarged, nor was the animal pregnant. The other ovary was of the usual size. The ovary about to be described was very much enlarged, being about 9:6:6 cm. The normal ovary of a three months' old calf is about 2:1:1 cm. In consistency it was elastic and hard, the surface smooth, without noticeable elevations. No

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follicles or corpora lutea were visible on the outside. The blood vessels, however, were prominent, and seemed to be very much thickened and varicose. On sectional view the connective tissue in the periphery was found to be much developed, and in the interior, also, there was much connective tissue. Near the middle was a space about 2 square cm. in size, which looked like corpus luteum tissue. From thence out toward the periphery were scattered smaller areas of yellow tissue, more or less resembling corpus luteum tissue, only more gelatinous toward the periphery. In the peripheral portion, but separated from the outside by connective tissue, lay round follicular bodies, frequently surrounded by a compact layer of connective tissue. They were filled partly with fluid blood, partly with a soft, gelatinous substance. These follicular bodies were all of a uniform size, about as large as a pea, perhaps somewhat larger. On a section through the middle of the ovary they were found in greater numbers. About eleven pieces from different parts of the ovary were cut out, and examined under the microscope. The examination revealed in the periphery a compact layer of thick connective tissue, along with greatly enlarged lymph vessels and blood vessels, whose walls were thickened and rich in connective tissue nuclei. There was no trace of germinal epithelium, nor were there any folds of germinal epithelium extending from the surface to the interior. Everywhere in the interior were to be seen connective tissue, blood vessels with thickened walls, and often enlarged lymph spaces, but nowhere small round-cell infiltration, or groups of polynuclear leucocytes.

In all the parts of the ovary, distributed throughout the connective tissue, we found corpus luteum tissue in different stages of development. In many places we found larger or smaller areas of typical well-developed corpus luteum tissue with capillaries between the cells. In some places we found areas of degenerated corpus

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luteum tissue, the cells without nuclei, presenting a scaly appearance, and interpenetrated by connective tissue nuclei. In other places the corpus luteum tissue had not assumed the scaly appearance, but showed a transition to what to the naked eye looked like a gelatinous mass, which stained red with eosin. In other places the tissue was filled with vacuoles.

Under the microscope the follicular bodies showed cells resembling those of corpus luteum, but the cells were usually somewhat different from the typical corpus luteum cells mentioned above. They gave evidence of transitions from typical lutein cells to those showing, by the use of hematoxylin and eosin, a protoplasm, which took up the color readily, and varied from cuboidal to cylindrical shape. There was connective tissue lying in the periphery of these follicular bodies, arranged in concentrix layers and full of cells. From the periphery capillary blood vessels radiated into the interior and along these, the cylindrical or cuboidal cells were arranged. In the periphery these cells were small, and often had a dark colored nucleus. They seemed to show transitions to the surrounding connective tissue. Toward the center they became larger. Often the round bodies were entirely filled with these cellular masses thus permeated with capillaries and then the structure of such a cyst resembles, in fact, that of an angiosarcoma, but frequently a partial disappearance of the cells took place, and the papillomatous character of the formation of this lutein tissue could readily be seen. The cells were formed around capillaries in which red corpuscles were often visible. In the periphery of these bodies were frequently seen rows of typical lutein cells, instead of simple connective tissue with blood vessels. In larger masses of connective tissue, which penetrated sometimes into the round bodies, we likewise found lutein cells formed around capillaries, and in such places we could see how the lutein cells were transformed into

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the cylindrical cells. It was the same kind of cell. This was very plainly seen in places where masses of typical corpus luteum tissue lay in close juxtaposition to the cell masses just described and merged one into the other. Now these papillomatous outgrowths degenerate, and become gelatinous masses, red stained with eosin.

Particular attention should be paid to the manner in which degeneration takes place. In the periphery of the cuboidal and cylindrical cells there remained the framework, as it were, red stained with eosin; the middle, however, was dissolved. We saw a similar change take place in smaller cells in the periphery, which apparently belonged to the connective tissue. It is well to again mention, that in the periphery the connective tissue showed in its structure every change to corpus luteum tissue. In one of these cysts the structure was very striking.

The papillomatous excrescences were much reduced in number, and consisted of some papillomatous elevations of the epithelioidal cells. Probably through the simultaneous growth of these epithelioid cells and the connective tissue, smaller secondary cysts had been formed, surrounded by the same cells. Growing diffusely, the character of the cells changed to that of large round cells, the protoplasm remaining only in the neighborhood of the nucleus. So we found larger or smaller masses of round cells in the connective tissue. In the center of the smaller masses such degeneration as described above as taking place in the cylindrical cells and in this way smaller cysts were in process of formation. But the lining of this larger primary cyst with such epithelioid cells was not complete. On one side the cells became flatter, then spindle-shaped, and finally could scarcely be distinguished from the neighboring spindle-shaped connective tissue cells, and then would appear an area with no epithelioid lining at all.

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In the interior of the cyst we found the above described gelatinous mass, red stained with eosin, as the remains of degenerated cells, besides the framework of the cells, corresponding to the peripheral parts of degenerating cells. These epithelioid cells spread out in all directions, and were seen in single rows and in larger groups in the connective tissue.

In these cysts there were also large blood masses and the remains of destroyed papillæ. The simplest explanation of this is, that the blood in the cysts resulted from the degeneration of the papillæ, which contained capillaries. Likewise in the vicinity of the first-described round bodies we found small secondary cysts of the same character as the primary cysts formed by the same cells. Primary and secondary cysts were separated by connective tissue. This connective tissue was, however, probably formed from the same cells as the inner epithelioid cells. The fibers were the same as those which later degenerated and then formed the framework to be dissolved. Only the nuclei were small and dark colored, and the fibers which formed the framework were well developed and not degenerated.

Then, too, in the surrounding connective tissue there were smaller spaces filled with blood, and on closer inspection we found in them sometimes the remains of degenerated epithelioid cells, which would seem to prove that here, also, there was a small new formation of these epithelioid cells, and that the extravasation of blood resulted from their degeneration. The cells of the cysts described were not essentially different from those found in the round corpus luteum-like bodies before mentioned, and also the whole structure of this cyst was not very different from the corpus luteum-like round bodies. But in the cysts we found open spaces which were lined with one layer of epithelioid cells, cylindrical and more or less regular. Where there were apparently more than one layer of the lining cells, it was the result of the

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pushing forward of a few cells. These cells had no cilia. They were the same cells as those whose relationship to the corpus luteum and probably also the connective tissue cells we have before mentioned.

Taking into consideration the macroscopic appearance of these small cysts, and the results of the microscopic examinations, there seem to be points in favor of the assumption that they have their origin in follicles. Yet we must mention some facts, which would seem to indicate the contrary.

We did not find any ova in these bodies—which, however, could hardly be expected, where the structure had been changed to such an extent. No ovum or normal follicle was found in the whole ovary. Further, the demarcation of the round bodies towards the periphery was frequently not so pronounced. We saw in these round bodies, particularly at the margin, not only newly formed capillaries, but strong blood vessels; also typical corpus luteum tissue with connective tissue growing into it; furthermore, in one place in the center of these bodies large spaces lined with endothelium. Again, these round bodies frequently showed a continuation into larger corpus luteum formations, without any intervening connective tissue, so that they seemed only a part of a large corpus luteum. They might be either places of greater cell growth in one large corpus luteum, or original ovarian follicles in which the corpus luteum tumor penetrates from outside or which themselves take an active part in this new formation of corpus luteum tissue.

One of the blood cysts which was examined microscopically, showed no epithelial lining, nor was there corpus luteum tissue around it. In the peripheral portion of the cyst firm connective tissue was found. Those parts were in the state of connective tissue organization. Deeper in the center we found spindle-shaped connective tissue cells. Around the periphery there lay yellow blood

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pigment granules. The explanation suggests itself that this cyst, which resembled the other so much in size and macroscopic appearance, was of a similar character. It is very probable that the villi were destroyed by the hemorrhage, or that the hemorrhage formed so early that the villi could not be developed at all. That there was no corpus luteum tissue in the vicinity proves nothing to the contrary, because we did not always find such around the other cysts. That might tend to prove that the corpus luteum cysts originated by primary growth of lutein cells, and that the blood cyst originated secondarily from the corpus luteum cysts. Whether that is true also of the other kinds of corpus luteum cysts described by former authors, is difficult to say, and certainly this explanation can so far be regarded only as hypothetical.

We must mention especially one more point in connection with the microscopic investigation: The finding of lutein cell groups and the corresponding groups of cylindrical and round cells in open spaces which were lined with endothelium, in the connective tissue. These open spaces were probably lymph vessels, and as we sometimes found blood in them also, they may have been, at other places, enlarged capillary blood vessels. These were especially seen in the neighborhood of the round bodies, but also more distant from them. In the vicinity of the above-described cyst of epithelial character, we also saw growing epithelioid cells in these open spaces resembling lymph vessels. In another place we saw all these growing cell masses (lutein cells and cells corresponding to them) directly bordering one side of an endothelial tube, and pressing the endothelial cells down into the interior. In another place we saw the cell masses directly penetrating into the lymph vessels. This took place particularly in the periphery of the follicular bodies, and this fact, together with the form of the cells at these places, makes it possible that these cyst-like formations are the beginnings whence, partly by direct

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penetration of the tissue, partly by transportation through the lymph vessels, such growths extend to different parts of the ovary. In one place where a hemorrhage had taken place we found a giant cell such as are found around foreign bodies.

Thus we have presented to us a new formation in an ovary, composed of tissue which has partly the character of typical lutein cells, and partly that of cells which show all transitional stages from lutein cells to cells resembling connective tissue. On the other hand, these lutein cells show every transitional stage to epithelioid, cylindrical cells, which in turn show changes first to masses of large round cells and secondly again, to cells resembling connective tissue cells, as well as to long rows of spindle-shaped cells as to cells that have more the cuboidal form and show in their periphery a well-formed membrane. In addition to these cells we see all possible forms of degeneration and liquefaction—for instance, from the vacuolar change of the lutein cells to dissolution of the protoplasm in the periphery cell—so that only the nucleus in the middle of the cell is seen, and around it a small mass of protoplasm, but of the outer part of the cell only a kind of membrane, staining red with eosin, is preserved. This degeneration may go further, so that only the membrane is recognizable, and finally only mucoid masses, not taking up eosin, are seen between the framework of connective tissue. Besides, the lutein cells may show a hyaline degeneration, in which the nucleus has been lost. On the other hand, we see the colloidal change of the cylindrical cells, in which process honeycomb-like meshes often appear as remains of the outline of the cell. We further see that this new formation penetrates into vessels—at any rate, the microscopic pictures are difficult to explain in any other way. This whole formation does not originate from the corpus luteum of pregnancy, because the six-month-old animal was not pregnant.

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This case is specially interesting for this reason, that it demonstrates the formation of epithelioid cysts from cells that probably are of connective tissue origin. According to older authors, such as Foulis, and among the more recent ones, Wendeler, even the follicular cells are of connective tissue origin. According to recent investigations it seems to be very probably that lutein cells are of connective tissue origin, at least among the higher mammalians, such as man, the cow, the hog. Koelliker, also, in his last publication, maintains the connective tissue origin of lutein cells among the higher mammalians. Sobotta and Van Beneden trace the origin of lutein cells from follicular cells in the rabbit, but these latter, too, as stated above, may perhaps be of connective tissue origin. The findings in the ovary under discussion would seem to go in support of the connective tissue character of the lutein cells, at least in the cow. Transitional forms between connective tissue and rows of lutein cells are present in large numbers. An identical degeneration of connective tissue in the interior of the papillæ and the epithelioid cells is also in favor of this assumption. Still, the microscopical appearance can make such a conclusion only probable, not absolutely conclusive.

But some points in this connection are doubtful: Whether the round bodies do correspond to follicles, or not; whether the new formation owes its origin to one follicle, or to many (provided the round bodies correspond to follicles); whether menstruation and the formation of the corpus luteum of menstruation had first to take place. Although the animal was so very young, still we can not exclude the possibility that menstruation had taken place. We must take into consideration the possibility that something else and not the rupture of a follicle may have been the exciting cause for this new formation.

There is still another point touching which we can make no positive statement. We found that the newly-

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formed cells were advancing and penetrating into the vessels. But we do not know whether or not other connective tissue also takes on the character of luteum tissue, and thus contributes to the new formation, or whether the change was originally limited to certain parts, most probably to the *theca interna,* and that then all these cells began to grow towards the center of the open space of the follicle, and also outside of it. Taking into account the arrangement of these round bodies and of the blood cysts of similar size to be found among the other cysts, and also the fact that especially the cells around these round bodies grow into lymph spaces, and that the growth of round cells form secondary cysts and grow diffusely into the surrounding tissue, it seems more probable that many cysts underwent this change which might have started in the *theca interna.* In this way could be explained the great variety of the growth seen in different places. This tissue carried away by the lymph spaces might start new formations of a similar kind in more distant parts of the ovary.

The literature upon such changes in the ovary as are described above is rather small. Changes as described in the ovary of the calf I have not found mentioned thus far. Rokitansky first observed a carcinoma of the corpus luteum, but no microscopic description being given, the case can not very well be used. Afterwards a number of authors, like Slavjansky, Nagel, Bulius, E. Fränkel, L. Fränkel and Orthmann, described corpus luteum cysts, partly with epithelium, partly without, partly filled with blood, partly filled with a lighter fluid. These cysts were larger than those described in the ovary of the calf, and they were single cysts. Recently Schaller and Pfoerringer have also described multiple, smaller cysts in an ovary which contained one continuous growth of lutein cells, but the cysts described by these authors were without epithelium. Schaller and Pfoerringer observed especially the situa-

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tion of the lutein cells along the lymph vessels. In their case they did not find the growth of the cells in the form of round cells. In a similar case of M. Voigt a like growth of lutein cells as in the second case seems to have taken place. There was a central degeneration of the tumor. The cells, which were like lutein cells, were arranged around capillaries. He therefore describes the tumor as a perithelioma, derived from corpus luteum tissue.

Especially interesting are the recent observations of Kworostansky, who found lutein cells in the wall of epidermoidal cysts. There was no connection of the cysts with the germinal epithelium. On the surface of the ovary also there was a patch of tissue with typical corpus luteum structure. These observations of Kworostansky in connection with the pictures here described, suggest that possibly other epithelial cysts may have the same origin as those we have described.

As to the manner in which the ordinary corpus luteum cysts are formed, two views are held. Most authors assume that the cysts originate by hemorrhage into the corpus luteum, or by transudation of the fluid from the vessels of the corpus luteum layer into the center of the cyst. But E. Fränkel explains the origin of corpus luteum cysts by growth of the follicle epithelium. Our cysts have not the typical structure described by the former authors, of the corpus luteum cysts. They certainly are very similar, however, and may possibly represent earlier stages. In that case our findings would support Fränkel's view. We certainly found a marked proliferation of the epithelioid cells.

SUMMARY.

1. The first described ovary, that of the six-month-old calf, proves that this new formation of tissue similar to corpus luteum tissue is not necessarily dependent upon the formation of the corpus luteum of pregnancy.

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Possibly this new formation is not even dependent upon the rupture of a follicle.

2. We see that these masses of lutein cells penetrate through the endothelium of lymph vessels, and in other places we see such masses of cells lying in the connective tissue in open spaces, which are lined with endothelial cells, capillary blood and lymph vessels.

3. The cells which compose this new formation show every transition in shape from cells similar to connective tissue cells to corpus luteum cells, to epithelioid cells lining the cysts. These lutein cells are, therefore, able to form the epithelioid lining of such cysts, and to assume the shape of columnar cells. It might be taken into consideration whether the epithelium of the epithlioid corpus luteum cysts have not a similar origin.

4. From the cells lining the ovarian cysts of the calf, a diffuse growth of round cells penetrates into the vicinity, and secondary cysts are formed by degeneration of the central cells.

5. Whether the new formation starts from one point or from many follicles simultaneously, can not be decided with certainty, though the structure of the round bodies would seem to indicate that they represent follicles in a state of growth. The fact that such a thick layer of connective tissue separates these round bodies from the surface of the ovary makes it improbable that the follicles have all been ruptured before growing, provided these round bodies represent follicles. In favor of the explanation that these round bodies are the starting point of the growth, we may adduce the fact that we find especially in the neighborhood of these follicular formations lutein cells penetrating into lymph spaces.

6. The majority of the recent authors derive the lutein cells of the higher mammalians from connective tissue cells of the *theca interna*. Therefore, connective tissue cells might be able to produce the epithelial lining of cysts. But we must also take into consideration the pos-

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sibility that other connective tissue cells besides those of the *theca interna* might participate in this growth, and that a change that ordinarily only takes place in the connective tissue of the *theca interna* extends to other ovarian connective tissue.

7. The cells resembling lutein cells may form the lining of cysts.

8. These microscopical findings speak in favor of the view that the lutein cells are derived from the connective tissue; the results could only be reconciled with the origin of lutein cells from granulosa cells by assuming that the graunlosa cells penetrate diffusely into the connective tissue and then can not be distinguished from connective tissue cells or by assuming, with Foulis and Wendeler, that the granulosa cells are connective tissue cells, and that, therefore, the growth of granulosa cells might, under certain circumstances, produce connective tissue formations.

April 9, 1900.

DEMONSTRATION OF METASTATIC TUMORS OF THE PERITONEUM FOLLOWING A PAPILLARY CARCINOMA OF THE FALLOPIAN TUBE.

E. R. LE COUNT.

On December 15, 1899, through the kindness of Dr. Henry P. Newman, I participated in a report with him before the Chicago Gynecological Society, of a rare tumor of the Fallopian tube which was at that time supposed to be a papilloma notwithstanding the microscopic examination had already shown that in places the epithelium had invaded the muscular wall of the tube. Re-

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cently, Dr. Byron Robinson has had occasion to remove from the abdominal cavity these large growths.

Macroscopic.—They consist of three large masses and about a dozen smaller; altogether they weigh 1350 grams. The largest piece measures 16x13.5x4 cm. and is disc-shaped; on section it presents a granular surface which resembles somewhat adipose tissue. Its external surface is smooth except for tag-like, torn adhesions. Its concave side has a furrowed and trabeculated appearance. The next smaller in size is very irregular in form, measuring 12x10x5 cm.; it is very rough and nodular externally and in spots has been torn. The smallest of the large pieces measures 11x7.5x4.5 cm., and on section is found to possess a much softened, necrotic center. One of its flat surfaces is quite smooth. All of the smaller masses are very irregular; some appear to be little more than fibrous tissue, others resemble the larger masses.

Microscopic (continued).—Sections were made of all the large growths, and some of the smaller, and stained by various methods. A large part of all the growths consists of necrotic tissue; many sections contain little else. The necrosis is most marked in and around the central portions; such necrotic tissue stains lightly or darkly, according to the degree of chromatolysis; varying degrees of edema and quantities of fibrin occur as well as small hemorrhages. In sections where necrosis is less marked the appearance of the innermost parts of the tubal tumor are duplicated; here occur cross-sections of papillæ lying in the necrotic tissue, which are in all respects similar to those in the tube in size, shape, paucity of stroma and number of epithelial strata; the epithelial cells contain similar large nucleoli. Karyokinetic figures, however, are much more numerous; often three, four or six dividing nuclei are present in a single field of the immersion objective (celloidin sections 15 to 20 mikrons thick). The stroma of the papillæ—connective tissue stalks—has its origin in a capsule which surrounds

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each metastatic growth more or less completely. The capsule is formed by long cells arranged parallel to the circumference, whose oblong nuclei contain nucleoli which are barely visible; these cells are not arranged in layers, for the nuclei have been cut in all possible diameters; the cells resemble the "fibroblasts" of organizing granulation tissue. In sections of the various metastatic growths, and even in different sections of the same growth, the capsule shows large blood vessels, regions of necrosis and of hemorrhage and thrombosed vessels. In regions just internal to the capsule, where the papillomatous growths have been so luxuriant that the papillæ are in contact and a tissue has been produced which appears solid and granular, if the stroma be examined in such places the connective tissue cells also are found with mitotic figures. They are never as abundant as the dividing nuclei of the epithelium; that the stroma or supporting tissue contains cells which are multiplying is beyond doubt; that these cells are the same as those which constitute the stroma is also certain, since all stages of multiplication by indirect division may be found, and also for the reason that there are no other cells in the stroma with resting nuclei than those described. It may be inferred that this difference between the stroma of the papillæ in the primary tumor and that in the papillæ of the metastatic growths is due to more favorable conditions of nutrition; it is also possible that the more rapid proliferation of the epithelium, as is shown by the abundance of dividing nuclei, has in itself led to a proliferation of the cells of the framework, and that this has been sufficient in amount to allow the observation of occasional dividing nuclei in the stroma cells.

This condition of embryonal stroma and embryonal epithelium, since both contain dividing nuclei, has resulted in a line of demarcation where epithelium and connective tissue meet, which is much less distinct than

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similar lines of contact in the primary tumor. In regions close to the capsule, where there has been a rich growth of papillæ and necrosis has not occurred, the indistinct line of contact and the entanglement of papillæ renders it difficult to distinguish between epithelium and connective tissue. Some aid may be had from the columnar position of the nuclei of the epithelium on the stroma, but this does not always obtain; in other places the epithelium has contracted away from the stroma so that a narrow space is present. The blood vessels in the stroma have very little wall; they resemble the vessels commonly encountered in a small spindle-celled sarcoma.

These specimens are remarkable in the close analogy they show with the primary tumor and also in the occurrence of proliferation of the stroma, as is shown by unmistakable karyokinetic nuclei. Hauser has reckoned that the dividing nuclei in certain carcinomata of the alimentary canal occur in the stroma, in the ratio of 1 to 500 of those in the tumor cells. These specimens are also interesting since they show a great similarity in structure to the tumors of the abdominal cavity that are secondary to carcinoma of the ovary; they are also examples of metastasis by implantation—mural implantation. Invasion of the surfaces adjacent to the open external end of the tube took place.

April 9, 1900.

EMBRYONAL RENAL ADENOSARCOMA.

MAXIMILIAN HERZOG AND DENSLOW LEWIS.

Among the tumors of the kidney we find very peculiarly interesting types having a very peculiar histogene-

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sis. We may mention in this connection those neoplasms arising from inclusions of displaced suprarenal tissue, known now more generally as hypernephroma. There is a type of mixed tumors of the kidney which has been attracting attention for a number of years, the true character of which, however, has been fully recognized only quite recently. These mixed renal tumors occur very early in life, frequently during the first years. They are not very common, but comparatively rare. They generally first attract attention not by any urinary symptoms, particularly not by hematuria, but by the increasing size of the abdomen. They grow very rapidly, speedily lead to general malignant cachexia, and destroy the life of the victim either with or without the formation of metastases. These tumors always develop inside of the kidney; the kidney tissue proper, however, does not take part in the proliferating neoplastic processes, but becomes compressed by the new growth and atrophic. Uriniferous tubules and their lining epithelia disappear in consequence of pressure atrophy. What is left of the kidney sometimes sits on the tumor like a flat cap. In other cases neoplasms of this kind proliferate toward the pelvis of the kidney, projecting into it in the form of polypoid masses. These malignant renal tumors of early childhood are so heterologous in their histology that they have been described as carcinoma, sarcoma, endothelioma, rhabdomyoma, and under a variety of compound names.

We are indebted to Birch-Hirschfeld[1] for having first successfully cleared up the confusion which reigned as to these new growths. This author, in his paper on "Renal Tumors," points out that the common histological feature of these neoplasms is the fact that they present a mixture of epithelial-adenomatous and connective tissue elements, and that all of these are proliferating in a most extensive embryonal manner. In the description of these neoplasms Birch-Hirschfeld states that

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sometimes the character of an adenoma predominates, while the connective tissue elements are less prominent; at other times the opposite prevails. These variable conditions are found not only in different tumors, but in different parts of the same neoplasm. These tumors very frequently contain striated muscle fibers, which in some of the reported cases were present in so large an amount that the new growths were designated as rhabdomyoma or rhabdomyosarcoma.

These tumors do not tend to form early metastases, but, on the contrary, lead to the latter only after the growth has become so very large that it has by pressure broken through the capsule. The neighboring lymphatics are not affected even if the adenomatous type predominates. Speaking about the classification of these peculiar renal tumors, Birch-Hirschfeld says: "We can only classify as pure sarcomata such neoplasms as arise from a proliferation of archiblastic elements without any active participation of epithelial tissues. It appears, *à priori*, possible that there occur in the kidney sarcomata very closely related to the adenosarcomatous mixed tumors. These pure sarcomata presumably would arise from embryonal inclusions equivalent to those archiblastic elements, giving origin to the adenosarcomata, only that the former do not contain any glandular (epithelial) tissue. Tumors of this type might be considered as simple embryonal renal sarcomata."

Birch-Hirschfeld believes that the embryonal renal adenosarcomata take their origin from remnants of the Wolffian body, and gives Eberth credit for having been the first one to suggest this possibility with reference to embryonal tumors of the kidney containing epithelial elements. Eberth tried to explain the presence of striated muscle fibers upon the ground that the connective tissue of the Wolffian body was rich in embryonal muscle cells.

This point is, however, not well taken. The embry-

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onal tissue Eberth refers to gives rise to non-striated, but not to striated muscle fibers.

Birch-Hirschfeld, in advocating the view that the mixed renal tumors take their origin from remnants of the Wolffian body, says that such an origin would explain the intimate relation between the tumor and the kidney and pelvis on the one hand, and the lack of a true blending between kidney substance and tumor tissue on the other.

Since Birch-Hirschfeld published his article upon these embryonal renal tumors there has appeared another very important contribution upon this subject by Wilms,[2] and while we can not indorse all of this author's views on the histogenesis and histology of these neoplasms, we gladly recognize his as a most excellent and exhaustive study of the subject.

Wilms, in reviewing Birch-Hirschfeld's idea as to the histogenesis of these tumors, says: "Birch-Hirschfeld traces the origin of these tumors back to embryonic inclusions derived from the Wolffian body. However, I think that this attempt at explanation only accounts for the presence of epithelial elements, but the question remains unanswered whence arise the other heterologous elements such as striated muscle fibers, cartilage," etc.

On this point Wilms very appropriately says that the Wolffian body does not give rise to any striated muscle fibers, and that embryonic inclusions derived solely from the Wolffian body can not be considered sufficient to account for all of the constituents of the peculiar mixed renal tumors of childhood.

If one reads Wilms' comments, one first gains the impression that he repudiates entirely any attempt to make remnants of the Wolffian body responsible for these tumors, and that he looks for the histogenesis of them in embryonic inclusions from the myotomes. It appears settled that the myotomes are those embryonal structures which give rise to the entire system of striated muscles.

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Cohnheim, as Wilms himself states, had already given it as his opinion that the rhabdomyoma of the kidney arise from embryonic inclusions of myotome tissue. If one, however, discards the Wolffian body entirely and looks to the myotomes alone, one finds indeed the source of the striated muscle fibers and the cartilage, but not the origin of the epithelial structures which these tumors contain. To surmount this difficulty, Wilms, toward the close of his monograph, gives it as his view that the mixed renal tumors under discussion arise from inclusion of the very earliest embryonic development, namely, from an undifferentiated mesodermal tissue which later on, in normal embryonic development, gives rise to the Wolffian body and to the myotome. To support this view Wilms is compelled to assume certain metaplastic processe)s in the development of these tumors. But these metaplastic processes have not been observed elsewhere, nor can Wilms furnish the least proof that they do occur in the mixed renal tumors. Wilms assumes that the inclusion of the very early undifferentiated embryonic tissue, which later on would give rise to the Wolffian body and the myotomes, forms, when it develops the tumor, irregular masses of round cells. That the latter are differentiated into epithelial cells, nay, more, that these, first present in irregular masses, differentiate themselves later into epithelial glandular tissue. Wilms' own words with reference to this process are as follows (*loc. cit.*, p. 62): "The epithelial glands (Druesenschlaeuche) in the tumor, according to our view, are not of primary origin, but they arise from certain cells of an embryonal tissue still undergoing differentiation. They arise from cells in which, in consequence of our inadequate means, we can not see future epithelial cells, but which appear first as small round cells in an embryonic tissue."

This view of Wilms appears utterly untenable if one compares it with what is known about normal processes

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of embryonic differentiation. Where do we find in normal embryonic metaplasia or differentiation of the human embryo any process in which small embryonal round cells later on become epithelia, first aggregated in irregular masses, and these then giving rise to regular tubular glands?

Wilms, in contesting Birch-Hirschfeld's view (which we indorse), that the glandular formations are the primary structures, and that the irregular cell masses are derived from the glands, says: "Against the view that the regular gland spaces are primarily and the cell masses secondarily formed speak several factors. First, the most complete epithelial structures are mostly found in the middle of the tumor. While in the younger parts of the tumor, where we have the youngest proliferation, we only find rudimentary ("angedeutete") glands and large irregular cell masses. In other words, where we have a recent growth we have either only irregular masses of round cells or an attempt ("andeutung") at gland formation. . . . In one of our renal tumor cases we found in a detached focus in the suprarenal gland not a single regular gland space, but only cell masses which show the beginning of a glandular arrangement," etc.

These arguments, particularly the statement that the tubular arrangement of epithelial elements is most distinct in the oldest and not in the youngest parts of the tumor, do not at all speak in favor of Wilms' views. Quite the contrary, all the facts cited clearly indicate that the irregular cell masses are the product of a proliferation of epithelial cells which primarily had a tubular arrangement. It is one of the best known and now most uniformly recognized facts of neoplastic proliferation, that the metaplasia of the tumor cells becomes the greater the more removed the latter are in time and space from their original progenitors. Let us look at any malignant epithelial neoplasm. We find that the newly-

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formed cells first deviate comparatively little from the mother cells from which they sprang. The further we get away from the original starting point of the tumor the greater, as a rule, is the deviation from the original cell type. This state of affairs becomes generally best marked when we compare metastases with the original tumor. These points have been dwelt upon in a very exhaustive manner by Hanseman.[3] It is very clear that Wilms' detached focus of a renal tumor in a suprarenal capsule, which he cites as a proof of his theory, was a metastasis, and as such showed a large degree of anaplasia and metaplasia of the original tumor cells. While it is one of the most common occurrences to find in tumors a regressive metaplasia, which, as one of us[4] has pointed out elsewhere, may have the character of a truly atavistic metaplasia, it would be an unheard-of condition in malignant tumors to find such a progressive metaplasia as Wilms claims these renal tumors represent. There seems to be no reason for the adoption of Wilms' hypothesis. The very facts, as he describes them, speak against it.

To give our own views as to the histogenesis of these tumors, it is necessary to enter very briefly into a discussion of the development of the myotomes ("ursegmente") and of the Wolffian body ("urniere"). These structures are developed from the early mesoderm which is first differentiated into the myotome and the lateral plate. Between these structures there is formed a thin bridge known as the nephrotome ("mittelplatte".). In the latter the transverse excretory tubules of the Wolffian body, emptying later on into the Wolffian duct, are formed. While these tubules develop the nephrotome becomes entirely cut off from the myotomes. This is in short the normal course of events.

With reference to the embryonal renal adenosarcomata of childhood, we assume that they owe their origin to an inclusion which is formed in the following manner: The

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nephrotome is not cut off at the normal site, but in such a manner that a part of the myotome is severed from the main mass and remains in connection with the nephrotome. The separation may take place, so that only a part of the myotome proper is cut off, or a part of the sclerotome may likewise be taken along. If the former is the case, we have the matrix for striated muscle fibers only; if the latter occurs, we have also the matrix for cartilage. If now we assume that a part of the nephrotome (Wolffian body) to which tissues of the myotome proper, or the latter and the sclerotome have become adherent by an abnormal process of embryonic separation, becomes included in the permanent kidney, we have a matrix containing all those embryonic elements which occur in the mixed renal tumors, namely, striated muscle fibers, cartilage, other connective tissue elements, and epithelial glandular structures. The latter, of course, are derived from the excretory tubules of the nephrotome.

This explanation appears to us the most feasible one; it will account for the character of these peculiar renal neoplasms without compelling us to take refuge, as Wilms does, to metaplastic processes unheard of in tumor formation.

In examining these tumors it is also necessary to consider Brosius'[5] views, that the adenomatous tissue in those neoplasms is not truly epithelial, but of a lymphatic endothelial character. If this were the case, one could without difficulty understand an origin from inclusions of the myotomes alone, since the latter contain lymphatic tissue. A close examination of the glandular spaces and cell masses, however, shows that we are dealing beyond doubt with true epithelial elements. The sections show distinctly that the epithelial nests are sharply defined. They do not gradually fuse into the surrounding connective tissue as in an endothelioma. Wilms, who cites the view of Brosius as to the endothelial nature of the cell

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nests, only does so to at once discard it, as do other authors who have studied the subject.

The following is a short abstract of the history of the case which we want to report in this paper:

August 2, 1898. The child, operated upon by one of us (Lewis) on this date, was a female white child, sixteen months old, weighing 21½ pounds before the operation. The tumor weighed 5½ pounds. The circumference of the abdomen was 23 inches. The child, which had to all appearances been normal when born, developed well and was in good health until May, 1898. Then there was noticed some gastro-intestinal disturbance; however, no diarrhea. The child then vomited a black substance, and the parents thought that the child had swallowed a piece of the nurse's dress. Dr. Lewis saw the child in June; it was then suffering from a slight bronchitis, which disappeared after three days. About this time there was also noticed a marked swelling of the abdomen. This swelling increased rapidly, and the general health of the child began to fail. A diagnosis of tumor of the abdomen and later sarcoma of the kidney was made. A urinary analysis failed to show albumin or casts. On July 31, 1898, Dr. Walter S. Christopher saw the child in consultation. He concurred in the diagnosis of sarcoma of the kidney. The operation was performed August 2, 1898, by Dr. Lewis, assisted by Drs. Weller, Van Hook, and Henry Norton, and in the presence of Drs. Almon Brooks and N. H. Henderson. The abdomen was opened by a transverse incision over the most prominent part. The tumor had formed very numerous adhesions to the intestines. These adhesions were separated without rupturing the gut anywhere. The pedicle of the tumor was then ligated and the new growth removed. The abdominal incision was closed; an opening of about one inch was left, through which the gauze dressing protruded. When the operation was completed at 3 p. m. the child appeared to be in good

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condition; the temperature was below 100, the pulse good. A number of hours after the operation the child took some nourishment, which was retained. The gauze was removed twenty-six hours after the operation; no pus or blood. Thirty hours after the operation the temperature rose to 103, and within an hour collapse and death followed. The exitus occurred thirty-one hours after the operation. On the following day Dr. Lewis made a partial autopsy. The intestines were found moderately distended with gas, no rupture, no blood, no pus. No metastases were found in the abdomen.

The tumor after removal was more or less globular in general outlines, but somewhat flattened above and below and at the lateral surfaces. The largest diameter extends from side to side and measures 18 to 19 cm.; the largest circumference is 58 to 59 cm. A fairly strong, shining, transparent capsule, nowhere broken through, but intact, invests the neoplasm. The lower surface of the new growth presents a crater-like depression 3 to 4 cm. deep. An incision made at this place shows that we have here located what is left of the compressed remnant of the kidney. The surface of the tumor is coarsely nodular, in consequence of the fact that the neoplasm is composed of a number of roundish nodular masses which vary in size from a hazelnut to a fist. All these masses are surrounded by the common capsule. The larger masses, as can be seen on the incised surface, are again composed of smaller nodules, each one surrounded by fibrous connective tissue septa. The interior of the tumor generally shows a tissue of a fibro-sarcomatous character, but there are also places which convey the impression of carcinomatous tissue. These two kinds of tissues are not intermixed in a heterologous manner, but are, on the contrary, quite separate and distinct. The difference in the macroscopic appearance of different parts of the tumor is explained by the microscopic examination. The parts looking like a carci-

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noma are made up of epithelial nests and tubular structures, the parts having a fibro-sarcomatous appearance are composed of connective tissue elements.

The compressed remnant of the kidney substance proper forms a conical or pyramidal mass, the apex of which projects into the crater-like depression of the under surface. The base of the cone has a diameter of 6 cm.; the distance from base to apex measures 3 cm. One is able to distinguish in what is left of the kidney the cortical and the medullary substances. Kidney substance and tumor are very distinct from each other. It appears that the latter has nowhere actually broken into the kidney substance.

The microscopical examination shows that the tumor is composed of two different kinds of tissue, epithelial structures and of connective tissue elements. These two types of tissue are distributed throughout the tumor in such a manner that we find in some places a pure picture of an epithelial neoplasm, while other places present the type of an embryonal connective tissue neoplasm. There is nowhere found in the examination of many sections either an intimate blending or a chaotic mixture of the two different types of tissue. They remain, on the contrary, discrete, and each one strictly preserves its own type. In this manner there is created a strong impression that the two kinds of tissue had originated quite separately.

The epithelial elements present themselves in the form of alveolar nests surrounded by connective tissue. Very frequently one sees either more or less in the middle, or situated quite eccentrically in the cell nests, tubular gland spaces. The epithelia lining the latter have very typical vesicular nuclei, possessing a moderate amount of finely granular chromatin, which is distributed in a peripheral manner to the inside of the nuclear membrane. The cell body is cuboidal, the protoplasm of moderate amount. The lumen of the glandular spaces so

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formed has approximately the size of a larger uriniferous tubule. One also finds glandular lumina of greatly enlarged size. The interior of such large gland spaces is filled with desquamated cells in a state of hydropic swelling. Gland spaces are, however, not only found in the interior of solid cell nests, but outside of them. Such tubular glands are lined by epithelial cells of the character described, and these single rows of epithelia are directly surrounded by connective tissue. The majority of the cells forming the solid nests deviate to a certain degree from the type of the epithelia which line the gland spaces. The former possess more chromatin than the latter, and the increased amount of chromatin fills the nucleus more densely. The latter deviates quite markedly from the character of a typically vesicular nucleus, and looks more like a granular nucleus. The cell protoplasm of the cells of the nests is not cuboidal, but round. If one compares these cells with those lining the tubules which empty into the Wolffian ducts of human embryos about 12 to 14 mm. long, one is struck by the great similarity which exists between them. The epithelial nests show neither a fibrillar nor any other stroma, but the alveoli contain exclusively the cells described. These cells also never show transitional forms leading over to the surrounding connective tissue. Such transitional forms are, as is well known, always found in endotheliomata. But a picture which might create the suspicion that we are possibly dealing in our case with an endothelioma is not found.

The connective tissue areas of the tumor generally give the picture of a pure rhabdomyoma. A small amount of the striated muscle fibers of the tumor very much approaches the type of adult normal striated muscle. The fibers are cylindrical, the longitudinal, as well as the transverse striæ, are very distinct. The oval nuclei are situated on the sarcoplasm directly under the sarcolemma. In such places, where we also find other signs

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of degenerative processes, the muscle fibers just described show fragmentation, and they are broken up into the component discs. In general, however, the type which approaches very much normal muscle fibers is only rarely found, and the embryonal, not fully differentiated type, predominates to a large extent. The major part of the tumor is composed of fibers containing several large oval or rod-like nuclei. Whether these cells have a sarcolemma or not can not be made out. The nuclei are not on top of the protoplasm, but, as can be distinctly seen in transverse sections, inside of the sarcoplasm. The striation is distinct, but very fine. This second class of cells found in the rhabdomyomatous parts of the tumor shows the characters of striated muscle cells as found in the early embryo of mammals.

The muscle cells of this type unite to form bundles, and these interlace each other in an apparently irregular manner. The tissue so formed contains numerous small blood vessels. The capsule of the tumor consists of densely packed fibers and slender fusiform cells. Remnants of kidney tissue could not be found in the tumor itself, neither was cartilage encountered.

In concluding the microscopical description of the tumor tissue we want to again state expressly that the epithelial as well as the connective tissue elements show an exquisite embryonal type, which is rarely found so very well pronounced in tumors. Sections from the kidney tissue proper show well-marked degenerative changes in the epithelia, particularly in those lining the convoluted tubules. The cells are swollen, indistinct in outlines, the protoplasm is cloudy, and the nucleus either faintly stained or entirely absent. The lumen of the tubules lined with degenerating epithelia frequently contains granular matter, occasionally hyaline matter. Other tubules show a free lumen and normal epithelia. In places completely collapsed tubules are seen. The limbs of Henle show the least changes, and many appear

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normal. The most prominent changes are found in the glomeruli, the majority of which is atrophic. The change, however, does not consist in a true degeneration, such as, for instance, a hyaline degeneration, but in a true atrophy. The capsule of the atrophic glomeruli is likewise very small and surrounds the latter so closely that there is only left a small lumen. The small atrophic glomeruli are so densely studded with nuclei that it is difficult to distinguish them individually even in thin sections and with high power. The glomeruli appearing normal as to size, likewise show an increased number of nuclei. It appears that there has taken place in consequence of the insult of pressure a proliferative reaction of the vascular endothelium of the glomerular capillaries. Aside from this evident proliferation of vascular endothelia other proliferative processes are not manifest, particularly not with reference to the uriniferous epithelia. Inflammatory reaction is likewise not seen. There is neither an interstitial round-cell infiltration nor the presence of fibrous interstitial tissue. The changes found in the kidney tissue proper all appear to be exclusively the result of pressure and pressure atrophy.

January 8, 1900.

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ANGIO-SCLEROTIC ULCERATION OF CERVIX, UTERI AND VAGINA.

A. C. GILLAM.

The causes of vaginal ulcer are, briefly, gonorrhea, syphilis, carcinoma, tuberculosis, exhausting diseases, acute and chronic vaginitis, severe labor, foreign bodies, such as pessaries, etc., and arteriosclerosis.

Under circulatory disturbances as a cause, Grosvenor[1] has reported three cases, describing a thrombosis of the veins of the walls of the vagina. He also reviews the literature on vascular changes and considers fully ten cases reported by others, making a total of thirteen. The first of his three cases, a stonecutter's wife, age 32, presented the symptoms of Bright's disease, but no local symptoms; the second, a molder's wife, age 37, died with symptoms of intestinal stenosis and no complaint or examination of the vaginal condition was made; and the third case, a laboring woman, age 56, died with symptoms of Bright's disease without complaining of the vagina.

All these showed the vaginal mucosa red and congested and in the upper part especially numerous, round and oval, rather shallow, sharp-edged ulcers, measuring 2 mm. to 2 cm. in diameter. In the first case visible thrombi were present in the vaginal veins and in the left jugular vein. Microscopic examination of the ulcers revealed the superficial necrotic layers and thrombosis of the submucous and deeper veins with fibrin and leucocytes. No bacteria were demonstrated. In the second case the same conditions were found, but many cocci and bacilli were present in the necrotic layers. No microscopic examination was made in the third case.

1. Grosvenor: Phlebo-thrombotic ulcers of the vagina. Jour. Path. and Bact., Edinb. and Lond., Jan., 1898.

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Out of the ten cases reported by others the ulcerated condition, according to Grosvenor, was discovered in five at the postmortem examination in women whose ages ran from 50 to 76 years. Sclerosis of the local vessels was demonstrated microscopically. Senile and arteriosclerotic changes were the general findings.

Four of the five clinical cases were in patients aged 50 to 60; one operated for cancer, microscopically proved to be non-malignant and healed nicely. The others were obstinate, though one yielded to change of climate. Colpitis, pain and irritation were prominent symptoms in one of these cases. The fifth clinical patient was pale and anemic, aged 37, and suffered with great burning and irritation, and gave a history of three months' discharge. Healing followed excision. Microscopically, thickening and obliteration of the vessels were found.

The following complicated case is interesting. The patient, a married woman, aged 50, occupation housework, had been sick for five months. The first symptom was vomiting, sometimes a dark brown material, but never pure blood, occurring generally after eating. Loss of flesh was noted and some abdominal pain. A cough with some expectoration had existed for the last five months. Constipation was present. The physical examination showed emaciation; the skin wrinkled and dry; atrophy of muscles and weakness; pupils equal and reacting to light and accommodation; tongue cyanotic and dry, and covered with a white fur; lung expansion slight; moist râles and spots of impaired resonance; heart sounds weak. An indefinite mass to the right of the median line was recognized in the abdomen, which was somewhat tender. The cervical glands were palpable. The clinical diagnosis was carcinoma of the stomach. The patient died six days after entering the hospital.

The postmortem findings were: Dislocation and dilatation of the stomach; carcinoma of pylorus; secondary nodules around pylorus; infiltration into wall of trans-

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verse colon; carcinoma of vagina and cervix of uterus; syphilitic scars in liver; emphysema; bronchitis; broncho-pneumonia; fibrous pleuritis; chronic nephritis with atrophy from healed infarcts; senile arteriosclerosis; general marasmus.

The three principal findings are, therefore, carcinoma of the stomach, vagina and cervix; syphilitic liver and arteriosclerosis.

The stomach is vertical in position and reaches to within one or two inches of the pubis. The pyloric end is much lower than normal and dilated. There is a slight curve near the pyloric end, which is just beneath the umbilicus. The vertical measurement of the stomach is 27 cm., transverse 8 cm. The ascending limb of the curve is 9 cm. long. There is a thickening at the pyloric end with white fibrous tissue. The transverse colon is dragged down to the lower border of the stomach. No adhesions are present except at the side of the pylorus between the omentum and pylorus and between omentum and transverse colon, in which is a large whitish-yellow nodule the size of the thumb. The mucous membrane of the stomach is normal and covered with a moderate amount of turbid mucus. The stomach is thin. At the pylorus is a hard nodule and a circular hard infiltration 7 cm. long, which narrows the lumen. On the cut surface the thickened wall of the pylorus is 1 cm. thick at the thickest portion, and the mucous membrane is here occupied by shallow superficial ulcers with smooth, irregular margins. On the posterior serous coat of the pylorus are nodular, white, firm excrescences which are grayish-yellow on the cut surface. The mucous membrane of the large intestine is smooth and normal. Where the transverse colon was adherent to the pylorus are a few nodular masses in its mesentery, with some diffuse thickening of the wall at its mesenteric attachment.

The uterus and appendages are small. The uterus

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measures 4.5 cm. long by 1.5 cm. antero-posteriorly. The vagina shows on its upper part an irregular and low ulcer, which has destroyed the cervix of the uterus and which involves the entire circumference of the vaginal wall near the cervix. Its margins are irregular, slightly raised and rather firm. The floor of the ulcer is somewhat nodular and extends along the mucous membrane of the uterus 1.5 cm. The uterine mucosa involved is rough and reddish. In the vagina also are several discrete, smaller ulcers, 5 mm. to 1 cm. in diameter, located near the larger ulcer.

The liver weighs 1000 grams and is small in size. On the surface are irregular, depressed cicatricial areas, also an irregular fissure on the right border of the right lobe with adhesions. The surface is smooth and shows mottled yellowish and reddish areas. Some of the areas are pure yellow in color and have a definite capsule when cut into. On the cut surface the scars are seen to extend into the tissue for some distance, as does also the previously mentioned fissure. Several yellowish areas with capsules are seen throughout the liver substance. One of the yellowish areas measures 7x5 cm. and its margins are irregular. The cut surface has a nutmeg appearance. The lobules show a dark center and a yellowish periphery.

The heart is small and the superficial vessels convoluted. The endocardium is smooth and the valves normal, except the mitral valves, which show some yellowish spots. The heart muscle is firm and the papillary muscles show an increased amount of connective tissue in some places. The thoracic aorta shows irregular, yellowish, raised areas and areas of thinning of the walls and some areas of calcification, on some of which are thin deposits of fibrin. The coronary arteries are quite smooth.

Microscopically, the mucous coat of the stomach appears to be normal. In a few places are seen accumula-

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tions of leucocytes. The submucous coat appears to be normal. The muscular coat is thickened and the fibers are separated in several places by groups of cells, larger than leucocytes, possessing a granular protoplasm and oval or round nuclei. These cells occur in narrow rows between the muscular fibers and sometimes in groups. Larger circular masses of cells occur without definite arrangement.

A section of an enlarged mesenteric gland shows large areas of necrosis and epithelial cells occurring in rows and groups, displacing the lymphoid cells. The colon shows misplaced epithelial cells in the submucous coat.

The surface edge of the large vaginal ulcer shows considerable granulation tissue, as evidenced by the large number of embryonal cells seen in this portion, which are much more numerous in the uterine wall, where the granulation tissue is thicker. The infiltration with embryonal cells is not very deep, being quite superficial. The blood vessels in the superficial area are very much thickened and nearly occluded in places. Beneath the granulation tissue are numerous blood vessels with thickened walls and intima. Most of them are empty. No evidence of carcinoma cells can be discovered in several sections mounted from both vagina and uterus.

A section through one of the round ulcers in the upper part of the vagina shows the floor consisting of a granular, eosin-staining material in which lie large numbers of cells with small round and irregular deep-blue staining nuclei. The subepithelial layer of areolar tissue is wider than usual and contains numerous cells, spindle-shaped with rather large elongated nuclei. The blood vessels in this region have thickened walls and are filled with blood. In some the lumen is obliterated. The ulcer near the central part almost reaches the muscular coats, which show the intermuscular septa thickened by a connective tissue increase and fibroid changes in the mus-

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cles themselves, as shown by Van Gieson's stain. Inflammatory cells are found between the muscles and the blood vessels here also are congested, and some have obliterated lumens. No cancerous groups of cells or misplaced epithelial cells can be made out. Gram's stain reveals no bacteria.

No clinical symptoms or signs are recorded pointing to the genital lesions in this case also, but the statement is made that the apathetic condition of the patient made it difficult to obtain a good history.

This case seems to present an arteriosclerotic process as the probable result of a syphilitic infection, and is peculiar in having a well-defined carcinoma elsewhere in the body.

The direct cause of the ulcers in this case is, doubtless, the lack of nourishment produced by the obliterated and sclerotic vessels cutting off the food supply. As pointed out by others, a secondary bacterial infection is very apt to occur in such areas and convert a simple necrosis into an active process. In this case no bacteria could be demonstrated.

The direct influence of carcinoma in the causation of these ulcers has been ruled out histologically. The general cachectic and anemic condition, however, of the malignant disease might have favored their formation.

The fibroid and arterial changes shown histologically may be syphilitic in origin; but the incomplete history fails to rule out other local chronic inflammatory processes and other causes.

The one point to be emphasized is this—what is apparently a malignant ulcer may not necessarily be one. Careful investigation should always be made, since an antemortem discovery in the given case would have led, doubtless, to the same diagnosis as the gross anatomical, namely—carcinomatous ulcer of the uterus and vagina.

February 11, 1901.

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TUMOR OF THE UTERUS OF A SOW (ADENOCARCINOMA).

LEO LOEB.

The tumor was from the horn of the uterus of a sow and weighed 16 pounds. There were three or four blood cysts in the tumor, which was pale and encapsulated. Metastases in the sublumbar lymph glands, which were about six times larger than normal. The uterine cavity was preserved. No sign of present or past pregnancy.

Microscopically one saw on some places well-preserved glandular structures from which continuous and branching rows of cells originated, which were surrounded by a fibromyxomatous stroma. The large vesicular nuclei of these rows of cells multiplied so rapidly that the appearance of giant cells was established. One nucleus overlapped the other, no cell limits being visible. This cell multiplication took place by mitosis. Cells in mitosis showed cell limits. At some places these rows of cells resumed the appearance of glands. Besides, there were present rows of small mononuclear (sometimes polynuclear cells of different sizes, also eosinophile cells, with and without granulations. We find all transitions from such small mononuclear to large mononuclear cells, which also are occasionally arranged in rows. These cells had, perhaps, emigrated from the lymph and blood vessels. The larger ones show beginning fragmentation of the nuclei. Besides, there are present giant cells of the myeloplax type with large fragmented nuclei. The tumor represents an adenocarcinoma with an uncommon kind of cell multiplication, which is very extensive, without forming carcinomatous alveoli. Also the large size of the tumor with

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the regular arrangement of the new-formed connective tissue is uncommon, as also is the presence of the different varieties of leucocytes and myeloplaques.

November 12, 1900.

ATRESIA OF FOLLICLES IN OVARY.

LEO LOEB.

Microscopic sections were demonstrated showing the difference between the atresia of follicles in different stages of maturity; also microscopic sections of two ovaries of a guinea-pig in which all follicles presented the picture of hypertrophy of the epithelium and in which the atresia without exception started by the ingrowth of connective tissue and capillaries into the follicular epithelium. Two slides were demonstrated showing follicles in the process of atresia, each one of which contained two ova. In one of these two follicles both eggs showed progressive changes, in the other follicle one ovum was unchanged and well preserved, the other ovum was segmented. In a third atretic follicle, of which a slide was shown, in which three ova were present, two of these were unchanged, the third ovum had undergone certain changes, the exact nature of which could not with certainty be determined. Another specimen showed a structure resembling very much a small corpus luteum, in the center of which, however, two successive sections demonstrated the presence of an ovum. At present it must be left undecided, if in this case the ovum of a ruptured follicle was retained and a corpus luteum had formed around it, or if under certain conditions a follicle

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which had not ruptured previously might in the stage of atresia give rise through hypertrophy to a structure similar to a small corpus luteum.

May 13, 1901.

RENAL TUMORS.

DANIEL N. EISENDRATH.

Two specimens of renal tumors were exhibited, one belonging to the variety of endotheliomata, or as they are frequently called, perivascular sarcomata, involving chiefly the lower half of the kidney, especially towards its anterior aspect. The predominating clinical symptoms had been those of a tumor the size of a child's head at term, felt in the right hypochondrium, distinctly movable with respiration; hematuria, and some chills, with rise of temperature. The kidney had been extirpated by Dr. E. W. Andrews. Patient was a man about 50 years of age. The other renal tumor, one of spindle-cell sarcoma, was removed by Dr. L. L. McArthur, and was a little larger than an adult head. Recurrence in both cases is certain to occur, as in one there was extension by continuity along the vessels, and in the other into the surrounding connective tissue.

November 13, 1899.

EMANUEL FRIEND presented specimens from a case of cyst-adenoma of the ovary. Patient 31 years old; mar-

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ried five years; never been pregnant; menstruation regular and painless; family history negative. About eight years ago severe pain developed in the region of the left ovary, but upon examination this was pronounced healthy. About one year ago a swelling appeared, extending from the symphysis pubes to the umbilicus, but this gave no pain until about a month ago. She then entered the hospital and at operation there was removed from the right ovary a small multilocular cyst. The patient made an uninterrupted recovery and was discharged from the hospital yesterday.

Adenomas developed as a result of disturbance in the formation of Pflüger's tubes in the growing ovary. Cyst-adenomas are simply adenomas which have undergone cystic degeneration; they consist of long, round, tortuous cavities separated from each other by connective tissue. These cavities may become obliterated entirely or partially by papilliform growths.

June 10, 1901.

E. R. Le Count demonstrated two specimens of benign hypernephroma.

May 14, 1901.

Weller Van Hook demonstrated a primary carcinoma of the male urethra.

November 13, 1899.

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THE LYMPHATIC SYSTEM.

SPLENECTOMY IN SPLENIC ANEMIA OR PRIMARY SPLENOMEGALY.

MALCOLM L. HARRIS AND MAXMILIAN HERZOG.

At present little is actually known concerning the physiology and pathology of the spleen. All cases, therefore, which may possibly aid in the elucidation of either or both of these subjects should be carefully studied and placed on record. The cases which form the basis of this contribution will be given in detail first.

CASE I.—Miss E. O., 22 years of age, born in Chicago of Swedish parents. The family history throws no light on this case. The father and mother, two sisters and one brother are living and in good health. One sister died of convulsions at the age of 3 years. There is no history of tuberculosis or malignant disease in the family.

When about 6 or 7 years of age she had measles and a very mild attack of diphtheria. At 11 she had quite a severe fall from a swing. She was perfectly well thereafter until about the age of thirteen years, when she felt a sense of discomfort about the stomach, and accidentally discovered a tumor in the left side of the abdomen. She told her mother about it, but she thought it would disappear, and nothing was done.

Some six months after she discovered the tumor she had a severe sick spell lasting nearly three months. This was diagnosed by her physician as typhoid fever, but there may be some question regarding the correctness of this diagnosis, as the course of the disease, if typhoid, was very atypical.

The illness began with profuse hematemesis. There was pain in the abdomen with distention and fever, but at no time was there any disturbance of the bowels. During the course of the disease, which, as stated, lasted about three months, there were two other hemorrhages from the stomach, neither of which, however, was as profuse as the first.

Some four months after getting up from this sickness, or at the age of fourteen, she was brought to the surgical clinic of

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Dr. Harris at the Policlinic on account of the tumor in the left side. The tumor was recognized as an enlarged spleen and a blood examination made. As the case was an out-patient, no record of the blood examination was kept.

There was no leucocytosis, however, and, after excluding leukemia and other known causes of splenic enlargement, a diagnosis of idiopathic enlargement of the spleen was made. She was given arsenic, and improved much in general health. She was seen at intervals for about two years, then disappeared from view, the splenic enlargement remaining about the same.

At 15 she went to work in a store. At 16 she had another hemorrhage from the stomach, and was off work for a time. Menstruation began at the age of seventeen, and continued in a regular and normal manner. From this time on her general health gradually failed. She became pale, reduced in flesh, and so weak that at times she was unable to continue her work.

In February or March, 1899, she had an acute illness lasting from two to three weeks, and marked by fever, severe pain in the region of the spleen, distention of the abdomen with tenderness, particularly throughout the upper part. It is probable that at this time the infarct in the spleen and the adhesions to the omentum, subsequently to be mentioned, occurred.

In May she again applied to Dr. Harris. At this time she was quite weak and unable to work. The face appeared full and puffed, but the extremities were thin and the general weight reduced. The spleen extended from the seventh rib to a little below the crest of the ilium and about two to three centimeters to the right of the mid-line below the umbilicus. The characteristic notch in the border was easily felt. A brownish pigmentation was noted throughout the skin. This was marked about the face, neck, forearms, and particularly so over the abdomen about the umbilicus and extending down to the pubes. The skin of the abdomen had a distinctly mottled appearance. No pigmentation was noted about the gums or interior of the cheeks. No enlargement of any of the lymph-glands could be felt. The bowels were regular and the appetite, as a rule, good. The urine was amber in color, sp. gr. 1016; acid; no albumin; no sugar; microscopic examination negative. Blood examination showed:

Hemoglobin (Fleischl)	40 per cent.
Red blood-cells	2,631,000
Leucocytes	2650
Color index	0.70

No plasmodium.

A differential count of the leucocytes was not made at this time. The pulse varied from 90 to 100; temperature, 98.6 F., and respiration, 24.

The case was now recognized as one of so-called splenic

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anemia or primary splenomegaly, and splenectomy was advised as a curative measure. The patient readily consented to the operation, and the spleen was removed through a median incision, May 25, 1899. This spleen is minutely described later. The patient made an uninterrupted recovery. The blood count following the operation is of interest. At the end of the first twenty-four hours there were:

Reds 4,037,000
Whites 23,600

This increase in the number of red cells is probably only apparent, and due in part at least to the withdrawal of fluids as, during the first twenty-four hours, she was unable to take anything by the stomach, and the salt solution injected into the bowel was not retained. While this may partly explain the 50 per cent. increase in the red cells, it can not explain the enormous increase in the leucocytes, amounting as it did to nearly 800 per cent. At the end of the second twenty-four hours, during which the patient took much fluid, there were:

Reds 2,800,000
Whites 15,000

Third twenty-four hours:

Reds 2,780,000
Whites 11,560

From now on the reds slightly increased, while the whites steadily decreased in number, so at the end of seventeen days there were:

Reds 3,250,000
Whites 5688

The urine was examined daily. For the first three days there seemed to be an absolute increase in the amount of the urea eliminated. The urea amounted to 22.3 grams, while normally, according to her weight, there should have been but 18.4 grams. By the sixth day the urea had dropped to 12 grams, and remained at about that amount thereafter. At the end of thirty hours the temperature had reached 103.8 F. and the respiration 41, although the pulse remained at 100, just where it was before the operation. She continued to have a temperature varying from 99 to 101, occasionally 102, for about two weeks, when it gradually subsided. No local conditions could be found to account for the temperature, and the patient felt well.

Jonnesco (*Archiv für klinische Chirurgie*, Band lv. S. 330) says he has noticed elevation of temperature immediately after his splenectomies, which he attributed sometimes to pulmonary congestion. At other times no lesions were apparent, and he then thought it due to a reawakening of malaria in the system. Our patient had never had malaria, and the cause of the tem-

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perature therefore must remain unknown. The patient left the hospital June 19 in good condition.

The subsequent history of this case is as follows: After leaving the hospital she continued to improve, and gained about twenty-five pounds in weight. September 1, she resumed her work. October 1, she began feeling badly about the stomach, especially after eating. After a few days she had considerable pain in the region of the stomach and vomited quite a little blood. She was obliged to take to her bed. The pains and vomiting continued for several days, but after the first day there was no longer any blood in the vomit. There was considerable gas formation in the intestines and colicky pains. After a temporary improvement she had a relapse, and returned to the hospital under the care of Dr. Harris, November 30. She was having considerable pain in the abdomen with marked tenderness over the region of the pancreas. Everything taken into the stomach was vomited. Temperature ranged from 101 to 102.4 F. Rectal nourishment was instituted and the stomach placed at rest. Improvement began at once. December 3, the blood count showed:

Reds	2,432,800
Whites	12,243

Stomach nourishment was resumed in a few days, and as the bowel movements were very offensive guaiacol carbonate was given. Improvement was progressive, and she left the hospital in good condition, December 17. December 23, a blood examination showed:

Hemoglobin (Fleischl)	45 per cent.
Reds	3,173,440
Whites	9060
Color index	0.64

Differential count of the leucocytes showed:

Polynuclear neutrophiles	49.4 per cent.
Small mononuclears	23.4 per cent.
Large mononuclears	12.8 per cent.
Eosinophiles	14.4 per cent.
	100.0 per cent.

Attention is called to the very large percentage of eosinophiles.

Since this attack the patient has improved greatly in health and has had no further illness. During the past year she has been able to attend to her work and she has felt perfectly well, in fact, much better than she has for many years.

She has menstruated but twice since the operation, once in May, 1899, two days after the operation, and again in October, 1899, when she had the illness above mentioned. Since then there has been no sign of a menstrual flow.

When last examined, January 13, 1901, twenty months after

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the operation, it was noticed that the brown pigmentation of the skin, which was so marked before the operation, was rapidly disappearing. The face had a clearer and brighter color, and but a slight mottling, scarcely perceptible, remained over the abdomen. No enlarged lymph-glands were anywhere palpable. An examination of the urine showed nothing abnormal. The result of the blood examination was as follows:

Hemoglobin	60 to 65 per cent.
Red blood-cells	3,776,000
White blood-cells	5200
Proportion of whites to reds	1 to 726
Color index	0.71 to 0.78

Differential count of the leucocytes:

Polynuclear neutrophiles	268 =	53.6 per cent.
Large mononuclear	106 =	21.2 per cent.
Small mononuclear	53 =	10.6 per cent.
Eosinophiles	57 =	11.4 per cent.
Transitional eosinophiles	4 =	0.8 per cent.
Basophiles	5 =	1.0 per cent.
Undefinable transitionals	7 =	1.4 per cent.
	500	100.0 per cent.

In regard to the blood examination, Dr. Herzog, who made the count, states: "When the differential count was made on cover-glass preparations treated with triacid and with glycerin-eosin-methylene-blue stains some peculiarities were observed which deserve notice. It was frequently difficult to distinguish between the small and the large mononuclears, and the former in general seemed larger than usual. The four corpuscles appearing in the above list as "transitional eosinophiles were polynuclears with few and very small eosinophilic granules. The basophiles (1 per cent.) were of the type of large mononuclears or of cells of a transitional character, and they contained a moderate number of coarse granules which stained with methylene blue. As transitional were classified such cells which could neither be grouped under large mononuclears nor under polynuclear neutrophiles. It was noticed that the blood contained more indistinct, hazy shadows of degenerating leucocytes than are usually seen." A large number of microcytes were also noticed.

The points of interest in this case are:

Its long duration.

The marked brownish pigmentation which gradually disappeared after removal of the spleen.

The high temperature lasting for two weeks after the operation without known cause.

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The remarkable increase in the number of blood cells, both red and white, immediately following the operation.

The increase in the reds was succeeded by a fall, and this in time by a gradual increase in number, which was of a more permanent character.

The great reduction in the number of reds which accompanied the peculiar sick spell about six months after the operation.

The return of the reds to a fairly good number, which has remained now for more than a year.

The return of the leucocytes to the normal number, but with marked changes in the relative percentage of the different varieties.

The suspension of menstruation.

CASE II.—Mr. R., widower, American, forty-seven years of age. Traveling man by occupation. The family history is good. Both father and mother lived past eighty and died of heart disease. Five sisters are all living and well.

He had typhoid fever when three or four years of age and facial erysipelas twice, at the age of six and thirty respectively. Thinks he may have had some malaria at about the age of thirty, but was never very sick with it. There is no history of syphilis or gonorrhea, nor has he been a drinking man. About two years ago he had an attack of la grippe. With the exceptions noted, he has always been healthy and strong.

He dates his present trouble from January, 1900, when he began having pains in the abdomen in the umbilical and epigastric regions. The pains were not particularly severe, nor could any exciting cause be assigned. Later his appetite gradually failed him and he was troubled with nausea. He had but one vomiting spell shortly before he entered the hospital, but there was nothing having the appearance of blood in the vomit. Associated with his condition were a progressive loss of strength and flesh. His loss in weight amounted to from thirty to forty pounds.

When he entered the Policlinic Hospital, September 16, 1900, he was very weak and considerably emaciated. His skin was of a dull, dirty, yellowish color, almost cachectic in appearance, but there was none of the brown pigmentation noted in Case I. His appetite was not good, and he was troubled with nausea. The bowels moved nearly every day, but often not satisfactorily. There were no urinary symptoms.

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An examination revealed nothing abnormal about the lungs or heart. The liver was not enlarged. In the left side of the abdomen was a large mass extending downward from beneath the left costal arch almost to the umbilicus and nearly to the mid-line, which, from its shape, location, mobility, etc., was considered to be an enlarged spleen. There was no enlargement of any of the palpable lymph-glands throughout the body. The temperature was normal; the pulse averaged 92, and the respiration 26 per minute. Urinalysis showed:

Amount passed in twenty-four hours, 750 cubic centimeters.
Color, quite dark;
Reaction, acid;
Specific gravity, 1030;
Urea, 2 per cent.;
Albumin, none;
Sugar, none;
Bile, none;
Microscope, few oxalate of lime and urate crystals.

Blood examination:

Hemoglobin (Fleisch).....50 per cent.
Red blood-cells 3,364,000
White blood-cells 28,200
Color index.....0.74

The leucocytosis consisted in an increase in the polynuclear leucocytes. There were no myelocytes, no nucleated red blood-cells. No plasmodia were found. To sum up, we had here a case showing:

A markedly enlarged spleen without leukemia.

There was no malaria or other pathologic condition to which the enlargement of the spleen could be attributed.

There was a moderate degree of anemia with a diminished color index.

There was a progressive loss of strength and flesh.

Based upon these facts, a diagnosis of splenic anemia or primary splenomegaly seemed justifiable, and removal of the enlarged organ was advised. Splenectomy, therefore, was performed September 28, 1900. The organ which was removed will be described in detail later.

The patient progressed slowly to recovery without incident of interest until October 21, when he had severe pain in the abdomen with distention and vomiting, and the bowels refused to move. Obstruction from adhesions was feared, and reopening of the abdomen considered. Next day, however, the bowels moved all right, and all unfavorable symptoms quickly disappeared. He had no further trouble.

For ten days after the operation his temperature ranged from 99 to 100 F., once reaching 101 on the second day. There were no local conditions to which this temperature could be

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attributed, unless a slight bronchial irritation due to the ether was sufficient. There was no material change in the blood count during his stay in the hospital, although the tendency was to improvement. Thus a blood examination, October 19, 1900, showed:

Hemoglobin (gravity test)	62½ per cent.
Red cells	3,864,000
White cells	24,000
Index	0.80
Differential count:	
Small mononuclears	11.7 per cent.
Large mononuclears	9.2 per cent.
Polynuclear neutrophiles	78.0 per cent.
Eosinophiles	.8 per cent.
Transitional forms	.3 per cent.
Total	100.0 per cent.

Number counted 1000.

He left the hospital, Oct. 25, 1900, in good condition. He lives out of the city, but has since been heard from as doing well and attending to his business.

That these cases are not identical is likely, for it seems probable there must be some differences between a case running a rapid course of a few months with a marked leucocytosis and a case protracted over several years with a marked leucopenia. Still, the cases are sufficiently characteristic to warrant their classification under that group to which the provisional term splenic anemia or primary splenomegaly may be applied. The characteristic features of this group of cases are:

A considerable enlargement of the spleen.

An anemia usually of moderate degree accompanied by a low color index.

An absence of the blood changes peculiar to leukemia.

Loss of strength and weight; and, finally, it may be added that the condition is usually a progressive one with a tendency to a fatal termination. As a summary of the literature of the subject has been given so recently by Sippy (*American Journal of the Medical Sciences,* 1899, vol. cxviii, pages 445-570), and the differential diagnosis so thoroughly considered by Osler (*American Journal of the Medical Sciences,* 1900, vol.

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cxix, page 54), no attempt will be made to again go over this ground.

One statement, however, made by Sippy needs to be modified in view of more extensive experience. He states that the disease may terminate fatally in from five to six months, and that three and one-half years is the longest duration recorded. While the first part of this statement is probably correct, the last part must now be modified, as the disease in our first case had existed for at least nine years, and Osler reports several cases in which the condition had existed from five to twelve years.

Concerning the pathogenesis of this group of cases but little or nothing is known. It can not even be stated with certainty in which organ or tissue the first changes make their appearance, although the evidence thus far obtained seems to point with great probability to the spleen as the part primarily at fault. The changes which take place in this organ will be described in detail later.

The changes which take place in the blood, so far as known, consist in a diminution in the number of erythrocytes with a reduction in the percentage of hemoglobin, thus giving a lowered color index. So far as the leucocytes are concerned, there may be a leucocytosis (28,200, Case II) or a leucopenia (2600, Case I), usually the number is below normal. The differential count shows no characteristic changes.

After the removal of the spleen, however, a marked change is noted in the relative proportion of the different leucocytes, although the total number remains about normal. This change consists in a large increase in the percentage of eosinophiles. An eosinophilia has been observed in animals after removal of the spleen as well as in man ("Histology of the Blood," Ehrlich and Lazarus, 1900).

It requires some months for the eosinophilia to be-

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come marked. In Case I, seven months after the operation, the eosinophiles formed 14.4 per cent. of the total number of the leucocytes, and twenty months after the operation, 11.4 per cent. Another change noted is an increase in the percentage of the large mononuclears. In Case I, these, at the end of seven months, had increased to 12.8 per cent., and at the end of twenty months to 21.2 per cent. The significance or explanation of these changes in the relative proportion of the leucocytes can not at present be given.

While it is freely admitted that the cases so far recorded and the facts at present at our disposal are not sufficient to warrant any positive deductions concerning the histogenesis of splenic anemia, it may not be amiss to consider some points in this connection.

One of the important questions to decide is: Does the anemia precede and cause the enlargement of the spleen, or is it secondary thereto? Jawein (*Virchow's Archiv für Path. Anat.*, 1900, vol. xvi, p. 461) has shown that a pathologic destruction of red blood cells is always followed by an enlargement of the spleen. This was found to be true clinically as well as experimentally. By the introduction of erythrolytic substances (chlorate of potash) into the blood of animals he was able to produce an enlargement of the spleen at will, and, furthermore, there seemed to be a direct relation between the degree of enlargement and the number of red cells destroyed. He therefore concludes that the chief function of the spleen is to remove dead red blood cells from the circulation, and that such dead cells have the specific property of stimulating this function. Thus is explained the enlargement of the spleen which takes place in certain infectious diseases, chronic malarial poisoning, etc., conditions in which an abnormal destruction of erythrocytes occurs.

At first sight, it would not seem unreasonable to apply the facts brought to light by Jawein's experiments to

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splenic anemia; to suppose that, owing to some unknown cause, there was a persistent abnormal destruction of the blood cells, which dead cells, through their specific effect on the spleen, excite an enlargement of this organ.

While this explanation appears quite simple and specious, there are facts which speak strongly against it. The most forcible of these is the fact that apparently perfect recovery follows removal of the spleen. The erythrocytes immediately begin to increase in number and the general condition of the blood improves.

It is impossible to reconcile this with the supposition that the splenic enlargement is secondary to the anemia, that it is, in a sense, a hypertrophy due to increased activity. It seems, therefore, much more probable that the splenic enlargement is primary, be its cause what it may, and that the anemia is dependent thereon. This does not elucidate, however, the essential nature of the disease. Let us now consider the changes found in the spleen.

Macroscopic Description.—The spleen removed in our first case had retained its shape fairly well; it is enlarged in all of its dimensions. Its diameters are 21 by 13.5 by 7 centimeters. Weight, after having been hardened in 4 per cent. watery formalin solution, 1055 grams. The surface is smooth on the whole, except in a few places where it had formed adhesions to the omentum. The organ is harder in consistency than normal. A wedge-shaped infarct extends from the hilum to the upper surface. Capsule thickened.

The spleen in our Case II is of the typical spleen shape and uniformly enlarged in all of its dimensions. Diameters: 18 by 12½ by 6 centimeters. Weight, after having been hardened in a 4 per cent. watery formalin solution, 600 grams. Surface slightly uneven and wrinkled; capsule highly thickened; spleen tissue some-

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what firmer than normal, however not as firm as in Case I. The surface shows a few grayish white spots.

Histopathology.—In studying the histopathology of splenomegaly, one is confronted with the difficulty that there are still a number of disputed points in the histology of the normal spleen, and that normal human splenic material is almost beyond one's reach.

Among the latest contributions to the normal histology of the spleen are those of Bannwarth and Kultschitzky. The papers of Hoyer have not been accessible to us, and the latest contribution of Mall has very little bearing upon our histopathologic considerations.

Bannwarth,[1] from his investigations, comes to the conclusion that there exists in the splenic pulp an open intermediary blood space with a common blood and lymph circulation. The common blood lymph spaces in the splenic pulp are, however, generally not lined by endothelial cells.

Kultschitzky[2] gives the following summary of his views: "I now feel compelled (in opposition to views held formerly) to admit that there exists in the spleen an open blood circulation, as was first described by W. Müller. I am now adopting this view partly in consequence of the more recent contributions of Hoyer, G. Hoyer, Bannwarth, and Sokolow, and partly in consequence of my own personal observations. . . . We, therefore, find that older observations as well as those of the most recent date concerning the normal histology of the spleen establish the fact that there exists in its pulp open blood spaces. These latter are formed by connective tissue fibers and cells, and they partly show an incomplete lining with endothelial-like cells. Split arterial capillaries and small arteries pour their blood

1. Untersuchungen über die Milz Archiv für Mikroscop. Anat., 1891, Vol. xxxviii, p. 345, and Neuere Milzuntersuchungen, etc. Correspondenzbl. für Schweizer Aerzte, 1893, Vol. xxiii, p. 586.

2. Zur Frage über den Bau der Milz Archiv für Mikroscop. Anat., 1895, Vol. xlvi, p. 673.

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into the lymph clefts of the pulp. The blood here mixes with the lymph and the mixture is carried away by venous capillaries and veins."

If, now, after this consideration of the normal histology of the spleen, we turn to the histopathology of splenomegaly primitive, we find only few extensive and correct contributions to the subject.

It may be stated here that the histologic changes in splenomegaly consist chiefly in a proliferation of endothelial elements as they have been described very recently in a most excellent manner by Bovaird,[3] who, however, is not the first author to observe the endothelial hyperplasia in splenic anemia.

Gaucher described the endothelial proliferation in 1882 in a "Thèse de Paris," but he had then wrongly interpreted what he saw, and spoke of an "hypertrophie idiopathique de la rate sans leucémie," or an "épithélioma primitif de la rate." In 1892, however, he gives a somewhat modified description, and clearly states that the proliferated cells which he mentions are of connective tissue and not of epithelial origin. He describes these cells as "cellules nuclées d'aspect épithélial," and he says that they owe their origin to a "proliferation irritative des éléments conjonctifs sous l'influence d'une cause encore inconnue."

Picou, in 1895, reported a splenectomy for splenomegaly, and he also describes the large proliferated epithelial-like cells, and mentions that some contain two to three nuclei. He states these cells are endothelial cells, and he calls the condition of the spleen an "endothélioma primitif." Cornil, speaking about Picou's case, thinks that the condition is one of primary hypertrophy of the spleen with proliferation of the elements of the pulp.

3. Primary Splenomegaly Endothelial Hyperplasia of the Spleen, The American Journal of the Medical Sciences, October, 1900.

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Collier[4] reports a case of a child 6 years old in whom the spleen began to enlarge at the age of 2. At the postmortem the spleen weighed four pounds two ounces. The author states that on microscopic examination the splenic reticulum is seen to be replaced by very large endothelial cells. It is stated that an older sister of the child likewise suffered from a fatal enlargement of the spleen.

Williamson[5] reports a case of splenomegaly with microscopic examination of the spleen. The patient was a boy 9 years old, who was admitted to the Manchester Royal Infirmary on Feb. 15, 1892. A blood examination showed red blood corpuscles, 3,030,000; white blood corpuscles, 4000; hemoglobin, 22 per cent. July 14, 1892, the child died.

The histological examination was much complicated by the fact that the child died of typhoid fever. Strange to say, the author denies that death was due to typhoid, but the macroscopic and microscopic findings clearly show it. Postmortem examination demonstrated ulceration in ileum, perforation at the site of one ulcer, general peritonitis, endocarditis of the mitral valve. Microscopically the spleen showed fibrous trabeculæ much thickened, fibroid changes of Malpighian bodies, splenic pulp congested, and the sinuses contained large and small nucleated cells. The most striking feature was the presence of enormous numbers of large nucleated cells, each containing a number of red blood corpuscles. These large phagocytic cells, which are characteristic of typhoid changes, were observed by Billroth as early as 1862, and have been described fully recently by Mallory.[6]

4. A case of enlarged spleen in a child six years old. Transactions of the London Pathological Society, 1895, Vol. xlvi, p. 148.

5. Cases of anemia with great enlargement of the spleen, Manchester Medical Chronicle, 1893, Vol. xviii, p. 103.

6. A Histologic Study of Typhoid Fever, Journal of the Boston Society of Medical Sciences, April, 1898, also Journal of Experimental Medicine.

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Sippy in his case describes the histology of the spleen as follows: "The majority of the Malpighian corpuscles show only slight alterations. Many appear normal, others present a slight increase in the reticular tissue, and now and then a Malpighian body is found which shows considerable sclerosis. No marked degenerative changes are to be seen in the cells. The veins show a moderate increase in the connective tissue which surrounds them, areas are found where this increase is very marked. Fibrous tissue extends some distance into the splenic pulp, enclosing within its meshes lymphoidal cells, isolated and in groups. In many places the pulp appears normal; however, in general, it is apparent that the reticulum is considerably increased. Here and there are to be found areas of marked sclerosis containing lymphoidal cells in the meshes of the fibrous tissue."

We now come to the most recent publication upon the subject, namely, that of Bovaird, who reports two cases:

Case I was that of a girl who, at the age of 3 years, was first seen in November, 1896. Swelling of the spleen was diagnosed, and the blood examination gave the following result: Red corpuscles, 4,400,000; leucocytes, 9000; hemoglobin, 75 per cent. The child was again seen after three years (1899). The abdomen at the umbilicus now had a circumference of twenty-three and one-fourth inches. Examination of the blood was as follows:

Red corpuscles	4,180,000
Leucocytes	14,000
Hemoglobin	62 per cent.
Polynuclear	57.5 per cent.
Large lymphocytes	29 per cent.
Small lymphocytes	12.5 per cent.
Eosinophiles	1 per cent.

Case II was an older sister of Case I. When first seen in November, 1896, she was thirteen years old. Enormous swelling of spleen was present, which first began to show itself when the child was three years old.

Blood examination:

Red corpuscles	2,880,000
Leucocytes	4000
Hemoglobin	60 per cent.

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In 1899, or when sixteen years old, the splenic tumor was larger, and a blood examination showed:

Red corpuscles	3,550,000
Leucocytes	7000
Hemoglobin	not given
Large lymphocytes	15 per cent.
Small lymphocytes	21 per cent.
Polynuclears	62 per cent.
Eosinophiles	1.4 per cent.

Splenectomy, May 17, 1899; death three hours after the operation. Spleen after removal weighed twelve and one-half pounds. Shape in general that of a normal spleen.

Bovaird in his very extensive microscopic descriptions states that the pulp spaces are much enlarged, lined by large endothelial cells, and often contain masses of proliferated endothelia. There are also found polynuclear giant cells. On other places there is found a fibrous connective tissue, and pictures are seen which suggest the transformation of the large endothelial cells into fibrous connective tissue. The abdominal lymph nodes and the lymph clefts of the liver likewise show masses of proliferated endothelial cells.

The author raises the question: Is this a diffuse endothelioma of the spleen with metastasis in the abdominal lymph nodes and the liver? This he answers in the negative. He considers the changes in the spleen those of a diffuse endothelial hyperplasia, and believes that the same morbid influences which caused the splenic changes also produced an endothelial hyperplasia in the abdominal lymph nodes and in the liver.

Histopathology of Our Own Cases.—(The material which had been hardened in dilute watery formalin was embedded in paraffin, and the sections were studied with a variety of stains.) Case II shows the changes which have taken place much clearer than Case I, so its microscopy will be described first and more fully.

Case II.—The capsule of the spleen is thickened and consists of a fibrous connective tissue, rather poor in nuclei. Weigert's elective stain shows a number of elastic fibers. The trabeculæ are likewise thickened and contain the same tissue elements as the capsule. The latter as well as the former contain a few involuntary muscle fibers. The Malpighian cor-

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puscles in general show few changes. Here and there evidences of a sclerosis are manifest. This is particularly seen in the cortical portion of some Malpighian bodies where the fibrous connective tissue is markedly increased and the lymphoid elements proportionately decreased. The most marked changes are found in the splenic pulp. The simple clefts of the pulp, partly and incompletely lined with endothelia, have disappeared, and all lumina seen possess a complete endothelial lining. The condition is such that it is impossible to say with certainty what has originally belonged to the capillaries and what to the pulp lymph-clefts.

The endothelia which line the common blood lymph spaces have not the character of normal flat vascular endothelia, but are cubical cells with comparatively large vesicular nuclei fairly rich in chromatin. The medium-sized cell protoplasm is finely granular and stains well with eosin. Quite a number of karyokinetic figures are seen in the endothelial cells. In some places the proliferation of these cells has been so lively Some of the cells contain two, three, and four nuclei. The that numbers of dropped-off endothelia are seen in the lumina. open blood lymph spaces also contain a large number of leucocytes, viz., lymphocytes, neutrophile polynuclear leucocytes, and eosinophiles. Red blood-corpuscles are not found in any numbers in the pulp spaces. This must be due to the fact that the blood was allowed to escape from the spleen after its removal. It is very probable that, as the blood ran out, almost all of the erythrocytes escaped, while the more sticky leucocytes were held back.

In spite of the fact that the open spaces are not completely filled, they are mostly found gaping and open. This is due to the fact that they have thick walls. This expression, however, is not quite correct. The wall proper of the spaces is really only formed by a single layer of endothelia, but the lumina are separated from each other by rather thick tissue septa. These show very little fibrous connective tissue, but are almost wholly made up of connective-tissue cells of an embryonal character, which, in appearance, are very similar to the endothelia described. Bovaird states that he saw in his case pictures which strongly suggest the transformation of the endothelia into connective-tissue fibers. Anything like this cannot be well seen in our case. But such a change is by no means improbable. The splenic pulp shows an abundant infiltration with hemosiderin and hematoidin. Large phagocytic cells containing included erythrocytes were not seen, but some of the endothelial cells contain hematoidin and hemosiderin granules.

Case I shows histologic changes similar to Case II. They

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are, however, not so clearly demonstrable. The pulp spaces are collapsed in many places, and the endothelial lining is not so uniformly present. The ischemic infarct shows the usual changes, namely, necrobiosis of the cellular elements with loss of staining properties of the nuclei. The tissues contained in the zone of the infarct still show to a large extent the original structure. The amount of fibrin found in the infarcted area is not large. The infarct thus appears of recent origin. Surrounding the infarct is a hyperemic zone with blood extravasation and migration of leucocytic elements into the ischemic area.

From the above description it appears obvious that the chief histologic changes found in splenomegaly consist in an endothelial proliferation, an endothelial hyperplasia. The French first looked upon the changes found in splenomegaly as an epithelioma, but later called it an "endothélioma primitif de la rate." Cornil has opposed this view, and so has Bovaird. We also wish to express our belief that the changes found in splenomegaly can not be looked upon as a diffuse endothelioma. We are of the opinion that the process is one resembling somewhat that found in lymphangioma. In the latter condition, as in splenomegaly, there is present a proliferation of lymphatic endothelia with enlargement and new formation of lymph spaces. The changes characteristic of lymphangioma have been described by Virchow, Klebs, Wegner, Tilger, Nasse, and others, and also by Herzog in a short paper published some time ago.

It appears to us, from its histopathology, that splenomegaly may be looked upon as a process similar to a diffuse lymphangoma. Ischemic infarcts either in the shape of one large infarct or as a number of small infarctions have been described a number of times in splenomegaly. These infarcts probably owe their origin to cell thrombi formed by the numerous leucocytic elements found in the enlarged lymph-blood spaces.

The next question which must engage our attention is: Can the pathologic changes in the spleen explain the progressive deterioration of the blood which is found

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in splenomegaly? It may be considered as established that red corpuscles are normally destroyed in the spleen. It appears at first sight not at all unlikely that red corpuscles are disintegrated in the spleen through the agency of phagocytic endothelial cells.

One is tempted to assume that an increase in the endothelial elements in the splenic pulp would be followed by an increase in the number of blood corpuscles destroyed. Yet, tempting as this hypothesis is in explanation of the progressive blood deterioration in splenomegaly, it lacks tangible evidence. We have in vain searched our sections for phagocytic cells containing red blood corpuscles; nor does the literature on splenomegaly contain any statement to this effect. The one case cited in which such phagocytic cells were found was complicated with typhoid fever, and therefore proves nothing.

Another explanation of the *modus operandi* of the destruction of red blood corpuscles in splenomegaly may be offered. The dissolution of senile blood corpuscles, or those damaged by toxic influences, may not be brought about directly by the phagocytic action of certain splenic cells, but by an erythrolytic enzyme formed in and secreted by certain splenic cells. If we assume that the endothelial cells of the splenic pulp furnish this erythrolytic enzyme, an easy explanation is offered for the great blood destruction in splenomegaly. These endothelia are enormously increased in splenomegaly, and if they do secrete an erythrolytic enzyme the latter would be increased very much. If we remove the spleen, we remove the source of the increased amount of the erythrolytic enzyme, and the blood destruction comes to a standstill. It is also obvious that there must be other organs—the lymph nodes—which have a moderate erythrolytic function, which comes into play more prominently after splenectomy. It appears, however, that the lymph nodes can not completely substitute the erythro-

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lytic function of the spleen. It was noticed in our Case I that twenty months after splenectomy the blood contained quite a number of indistinct, hazy blood corpuscles, and many microcytes.

One thing appears certain, namely, that the changes in the spleen must in some way be responsible for the blood deterioration in splenomegaly, otherwise removal of the changed spleen would not be such an excellent therapeutic measure as it appears to be.

Treatment.—The treatment of splenic anemia from a medical standpoint has not proved successful. Attention is therefore particularly directed to the value of splenectomy in this class of cases.

Sippy gives an incomplete list of cases of primitive splenomegaly in which a splenectomy was performed. He cites the following cases:

CASE I.—Operator, Spencer Wells; date, 1865; female, aged thirty-four years; weight of spleen, 2672 grams. Result: Death.

CASE II.—Operator, Péan; date, 1876; female, aged twenty-four years; weight of spleen, 1125 grams. Result: In one month patient had recovered perfectly; subsequently died of toxic enteritis.

CASE III.—Operator, Czerny; date, 1878; female, aged thirty years; weight of spleen not given, size, 23 by 12 by 8 centimeters. Result: Complete cure.

CASE IV.—Operator, Franzolini; date, 1881; female, aged twenty-two years; weight of spleen, 1526 grams. Result: Complete cure.

CASE V.—Operator, Frascani; female, aged sixteen years; weight of spleen, 1310 grams. Result: Death from hemorrhage in four hours.

CASE VI.—Operator, Ceci; date, 1893; female, aged thirteen years; weight of spleen, 1300 grams. Result: Recovery.

CASE VII.—Operator, Lindfors; date, 1892; female, aged twenty years; size of spleen, 25 by 15 by 7 centimeters. Result: Recovery.

To this list the following cases have to be added:

Banti (Splenomegalie mit Lebercirrh. Ziegler's *Beiträge*, 1898, Vol. xxiv, p. 21) reports three cases of splenomegaly with cirrhosis of the liver, operated upon by F. Colzi.

CASE VIII.—Operator, Colzi; woman. Result: Died several

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days after the operation from a septic puerperal complication.

CASE IX.—Operator, Colzi; young man. Result: In best of health thirty-three months after the operation.

CASE X.—Operator, Colzi; woman. Result: Was in good health twenty-one months after the operation. No anemia.

CASE XI.—Operator, Power (Successful removal of an enlarged and displaced spleen. *British Medical Journal*, 1900, November 17, p. 1428); widow, forty-three years old; operated September 6, 1899. Three and a half years ago she struck her left side just over the lower ribs. Two years later she noticed the lower part of her abdomen increasing in size. At the operation the spleen was found suspended from a pedicle four inches long, consisting of fatty connective tissue with large veins and splenic artery. After removal the estimated weight of the spleen was two and one-half pounds. It weighed seventeen to eighteen ounces after having been in alcohol for six months. The blood examination eight days after the operation showed:

Red corpuscles	4,230,000
White corpuscles	17,000
Lymphocytes	18.75 per cent.
Large mononuclear	12.5 per cent.
Polynuclear	65.5 per cent.
Eosinophiles	3.5 per cent.

No myelocytes.

The patient recovered.

CASE XII.—Operator, Cushing (Splenectomy for primary splenic anemia. *Maryland Medical Journal*, Baltimore, 1899, Vol. xli, p. 140). The short report states that a splenectomy was made for splenic anemia. Patient made a good recovery and gained thirty pounds in weight.

CASE XIII.—Osler. Man, aged thirty-three years. Trouble of ten years' duration:

Red blood-corpuscles	3,000,000
Leucocytes	2800
Hemoglobin	25 per cent.

Differential count:

Polymorphonuclears	84.4 per cent.
Small mononuclears	4.4 per cent.
Large mononuclears	5. per cent.
Transitionals	3.4 per cent.
Eosinophiles	2.8 per cent.

Splenectomy; patient recovered; continued well one year after operation.

CASE XIV is one of Bovaird's cases, which has been referred to more fully above. Girl, sixteen years old. Patient died three hours after the operation.

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CASE XV.—Picou (Epithélioma primitif de la rate de Gaucher. *Bull. de la Soc. Anat. de Paris*, 5e Ser., 1895, Vol. ix. p. 531 reports a successful splenectomy in a woman thirty-two years old. The spleen weighed 2800 grams and was 26½ by 14.2 by 9 centimeters.

CASE XVI.—Gaucher (De l'hypertrophie idiopathique de la rate sans leucémie *La France Médicale*, 1892, Vol. xxxix, p. 529) mentions that among three specimens of splenomegaly which he examined, there was one in which the spleen had been removed by an operation. No further details are given about this splenectomy.

CASE XVII.—M. Tscherniachowski (Hilderbrand's *Jahresbericht für Chic.*, 1899, S. 720), a twenty-five-year-old woman. Duration of tumor five years, Diagnosed as essential hypertrophy of spleen. Splenectomy was performed on account of constant increase in the size of the spleen, with loss of strength in spite of treatment. Complete recovery.

To this list of splenectomies for primitive splenomegaly we can add the two cases above recorded. This then makes a list of nineteen cases, with fourteen recoveries, four deaths, and one case where the result is not stated. A mortality of a little over 20 per cent. This is certainly a very favorable showing for splenectomy.

There may be some question as to the propriety of including Banti's three cases in this list, but, as two of them recovered and were reported well thirty-three and twenty-one months respectively after the operation, it would seem that the splenomegaly was the primary and chief condition and the cirrhosis of the liver secondary thereto, and that they are therefore justly entitled to be included.

Concerning the after history of the cases that recovered, unfortunately, but little is said. In eight cases it is simply stated the patients recovered and were well, but the length of time after the operation at which the observations were made was not stated. In one case the time is specified as one year after the operation; in one case twenty-one months, and in another thirty-three months. It is to help fill in this gap that the subse-

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quent history of our Case I was entered into in such detail, as it has now been under observation about twenty-two months.

If it can be shown, as now seems probable, that these cases do recover after splenectomy, not simply recover from the operation but regain fully their health and well being, it will establish splenectomy as the proper line of treatment in these cases, as, up to this time, medicinal treatment is acknowledged to be unsuccessful. As the difficulties as well as the dangers of the operation increase in proportion to the size of the spleen, it is advisable to operate as soon as a correct diagnosis can be established and the futility of medicinal treatment is made evident.

Concerning the technique of the operation there is but little to add. The median incision is the one most desirable in the majority of cases. Most of the operators who have removed enlarged spleens recommend dividing the gastrosplenic omentum between the ligatures first, and freeing the upper end of the organ from the vault of the diaphragm in order to turn it out of the abdomen before ligating the pedicle proper. The difficulties in reaching the gastrosplenic omentum with an enlarged spleen in place are often very great, as most writers have stated; therefore, after attempting to follow this method in our first case, it was abandoned.

The incision was extended downward so that the lower end of the spleen could be drawn upward. The splenic vessels were then easily approached and ligated. The veins in these cases are enormously dilated, and so thin that they are easily punctured or lacerated in attempting to pass the ligature needle.

It is probably better to ligate at once than to place a large clamp on the vessels with the intention of ligating after the organ is removed, as the thin veins are apt to tear at the edge of the clamp during the subsequent manipulations, and great difficulty may be experienced

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in again getting control of the hemorrhage. This was experienced in the second case.

After ligating and dividing the pedicle, the spleen may be drawn downward and the gastrosplenic omentum more easily gotten at.

March 11, 1901.

GENERALIZED TUBERCULOUS LYMPHADENITIS, WITH THE CLINICAL AND ANATOMICAL PICTURE OF PSEUDOLEUKEMIA; THE STUDY OF A CASE.

THOMAS R. CROWDER.

During the last few years there has been a growing tendency among writers and observers to look upon Hodgkin's disease as of infectious origin. The staphylococcus and streptococcus pyogenes, the pneumococcus, and various less well-known organisms have been found in the glands—sometimes before death and sometimes after—and often investigators have not hesitated to attribute to this or that organism the causative rôle.

During the last ten or twelve years cases have been described as pseudoleukemia, agreeing clinically and showing after death lesions pointing to that disease, which careful investigation has proved to be tuberculous, thus establishing a form of tuberculous lymphadenitis so closely simulating pseudoleukemia that the two conditions are often indistinguishable even at the postmortem examination. Such cases have been reported by Weisshaupt,[38] Troje,[34] Brentano and Tangl,[4] Cordua,[5] Waetzoldt,[37] Dietrich,[10] Courmont, Tixier and Bonnet,[6] Sternberg,[31] and others.

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The number of cases is yet small in which research has been carried far enough to remove all doubt as to their nature, though the frequency of such a special class of infectious lymphadenitis is in all probability much greater than has heretofore been supposed or than methods used until comparatively recently could demonstrate.

The actual occurrence of tuberculosis in lymphatic glands is not easily determined by mere anatomical inspection. It is often difficult to say, even with the aid of the microscope, whether a given glandular hyperplasia is tuberculous or non-tuberculous in its origin. The classical cell group is certainly not a necessary product of the tubercle bacillus in tissue; hence the histological appearance alone is not always reliable in diagnosis. When the organisms are scarce, it may be difficult or impossible to demonstrate them. The remaining resource is the inoculation of susceptible animals and beyond the verdict of that experiment we are at present not able to go. In the older cases we can draw but probable conclusions in the absence of such experiments and of bacteriological examination, and investigation is desirable concerning tuberculosis as a primary general glandular affection and its relation to pseudoleukemia.

This contribution is based upon a study of the following case, diagnosticated clinically and postmortem as pseudoleukemia, and upon a review of the more important literature of the subject.

John A., 34 years of age, a lumberman by occupation, was admitted to the service of Prof. N. Senn at the Presbyterian Hospital of the city of Chicago, on Feb. 14, 1898. The following brief clinical history is taken from the hospital records: His father is living and healthy; his mother died of an unknown cause at the age of forty-five. There are three healthy brothers and one sister living; two brothers and one sister died of unknown causes. The previous history of the patient is that of continuous good health. He never suffered from any serious illness or injury. He uses alcoholics moderately. The present disease began in August, 1897, with swelling low down in the right side of the neck behind the sterno-cleido-mastoid

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muscle. Pain appeared in this region about December 25, 1897, with rapid enlargement and extension of the swelling to the right axilla. Up to the time of his admission about twenty pounds in weight have been lost. The bowels have been regular and no marked symptoms have been referable to any region. The only treatment was painting of the skin over the swelling with tincture of iodin.

Examination of the patient reveals a large swelling in the right side of the neck and a mass in the right axilla of the size of a hen's egg. The general nourishment is fair, the face pallid. The patient walks about the ward and all his muscular movements are free. (No mention is made of the chest, abdomen, or other parts of the body, and it is supposed that these regions gave normal physical findings.) Temperature 101.8 F., respiration 24, pulse 104. During his stay in the hospital the left cervical and axillary regions became the seats of tumor masses which underwent enlargement along with the masses present on his admission. The enlargement was not always progressive, sometimes a more or less marked diminution in size being noted. Measurements of the circumference of the neck are recorded, indicating a variation of more than two inches.

About the middle of May, 1898, the patient began to lose appetite and there was noted a decrease in the general nourishment. The morning temperature all through his early stay in the hospital was about normal, with an evening rise somewhat irregularly up to about 101.5 F. The pulse was usually about 100, ranging from 84 up and remaining above 120 after the 1st of March, 1899.

Up to the middle of March no abnormal findings in the urine are noted. About March 20, 1899, a profuse diarrhea developed and lasted to the time of death, which occurred with high temperature and delirium on April 27, 1899.

A week or so before his death an examination of the blood was made by Dr. J. A. Capps. It showed a specific gravity of 1.052; hemoglobin (Fleischl), 62 per cent.; red corpuscles, 4,320,000; leucocytes, 19,000. A differential count of 1000 leucocytes gave the following results: Small uninuclear, 30 per cent.; large uninuclear, 2.5 per cent.; polymorphonuclear neutrophiles, 67 per cent.; eosinophiles, 0.5 per cent. There were no myelocytes, no nucleated reds, no polychromatism and only a very slight poikilocytosis.

The treatment consisted in the administration of Fowler's solution in increasing doses, given by the mouth and injected into the tumor in the right cervical region. From Feb. 16, 1898, to April 9, 1898, fifteen minims of Coley's toxins were injected each morning into the tumor of the neck, the charac-

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teristic chill and slight temperature following each injection. An abscess was finally developed at the point of puncture. This was incised and healed slowly. No record of diminution in the size of the glands is recorded during this time. The patient received at various times exilir of iron, quinin, and strychnin, carbonate of iron, and various sedatives.

The postmortem examination was made on April 28, 1899, twenty hours after death.

ANATOMICAL DIAGNOSIS.—Hyperplasia of the cervical, submaxillary, axillary, mediastinal, peribronchial, and retroperitoneal lymphatic glands; lymphoid nodules in the liver, spleen, and lung; obliterative fibrinoplastic peritonitis; left hydrothorax; right serofibrinous pleuritis; edema of the lungs; bronchitis; cyst in the pelvic fascia; acute degenerative changes in the kidneys; chronic gastritis; beginning atheroma of the aorta; edema of the ankles; general emaciation.

External Examination.—The body is that of a well-developed, poorly nourished young man. Rigor mortis is absent. There is postmortem lividity of dependent parts, with well-marked edema of the feet and ankles. There is an area of superficial necrosis over the left trochanter.

A large, lobulated swelling occupies either side of the neck, raising the lobe of the ear, extending upward into the parotid region, downward to the clavicle, and forward from the anterior border of the trapezius to meet the other in the median line beneath the symphysis mentis. Similar nodular masses occupy both axillary regions, lifting the outer borders of the pectoralis major muscles and reaching as low as the nipple in the midaxillary line. A puckered scar 1 by 1.5 cm. in size occupies the most prominent part of the mass in the right side of the neck and in this region the skin is adherent to the deeper structures; in all other parts it is tense over the masses, but not adherent. The epitrochlear lymph nodes are not palpable. The inguinal nodes show no abnormal enlargement upon palpating through the intact skin. There are no palpable glands in the popliteal spaces.

Internal Examination.—The abdominal cavity is obliterated except for a small space in the pelvis, which contains about a pint of clear, rather thick fluid. Friable adhesions of a translucent gelatinous material bind the coils of intestine together, to the other abdominal viscera, and to the parietal peritoneum.

The pleural cavities each contain about 800 c.c. of straw-colored fluid; that in the right side contains small flocculent masses of fibrin. There are fibrinous adhesions between the right lung and the diaphragm and between the posterior part of the lower lobe and the chest wall. A few firm, strand-like, fibrous bands of adhesion bind the left lung to the diaphragm

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and pericardium, and the right lung is similarly held to the posterior mediastinum.

The pericardial cavity contains about 60 c.c. of clear fluid. The pericardium is smooth and free from adhesions.

The tonsils, tongue, pharynx, larynx, esophagus, trachea, and thyroid gland show no changes.

The heart is of normal size and smooth externally. The cavities are empty; the endocardium and valves are smooth and of normal appearance. The myocardium is uniformly brownish red in color, and of moderate firmness. The papillary muscles show no increase of fibrous tissue.

Throughout the whole aorta and the beginning of the coronary arteries are scattered a few smooth, slightly raised opaque yellow areas in the intima.

The left lung is smooth externally except for a few torn adhesions. The interlobar fissure is partially obliterated by fibrous tissue. The lung crepitates throughout and is rather light and spongy. The cut surface is grayish red, and shows a moderate amount of blood and some edema. There is mucopus in the bronchi. The peribronchial lymph glands are large and firm, and extend into the lung along the bronchi as tumor-like masses as large as walnuts. On section they are grayish yellow, with dark gray spots. Under the pleura of the middle of the lower lobe is a nodule 1 cm. in diameter; it is firm and of a uniform yellowish color. The right lung answers to the description of the left with the addition of fibrinous flakes and dulling of the pleural luster over the surface of the lower lobe. No subpleural nodules are noted in this lung; and in no part of either lung are there areas of consolidation or evidence of old or recent tuberculosis.

The masses of lymphatic glands in the axilla extend far back beneath the scapulæ, and are continuous beneath the clavicles with the large masses in the neck. The cervical chains extend downward along the sides of the esophagus and trachea into the mediastinum, along the bronchi into the lungs and on down connecting with the retroperitoneal chain (Fig. 1.). There is no enlargement in the glands of the retroperitoneal region below the promontory of the sacrum. Those above are large and firm. The individual glands are sharply circumscribed by fibrous capsules and rather loosely bound together by fibrous tissue; those underlying the scar in the right side of the neck are closely and firmly held by cicatricial tissue. They vary in size from that of a pea up to 7 cm. in diameter, the largest being found in the axillary regions. They are firm in consistence. On section they are dry and show a grayish color with rather well defined, irregular, yellowish areas. These areas are not like those of ordinary caseation; they are

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firm and not easily disintegrated. Scraping the surface yields no fluid.

The liver is moderately enlarged. The capsule is uniformly roughened by torn friable adhesions. Beneath the capsule over the posterior parts of the upper surfaces of both lobes are several pea-sized firm nodules, which on section are seen to be of spheroidal shape and uniformly yellowish in color. A few similar nodules are embedded in the substance of the organ.

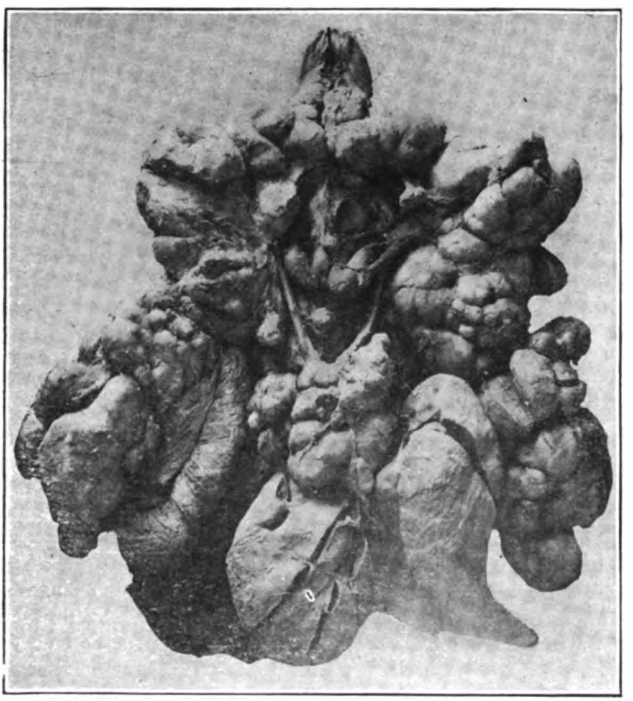

Fig. 1.—Anterior view of the organs of the neck and thorax, with the cervical axillary and mediastinal glands.

The lobular markings are fairly distinct, the parenchyma is rather pale and opaque.

The spleen is much enlarged, extending below and to the right of the umbilicus. It is of firm consistency and distinctly nodular over its entire surface, the nodules being of lighter color than the surrounding substance. On section firm yellowish nodules, varying in size from 0.25 to 2 cm. and of different shapes are seen to be scattered throughout the entire

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organ (Fig. 2). The lymph nodes at the hilus are much enlarged and resemble those already described.

The pancreas shows no changes on the cut surface. It is surrounded by many large lymph glands.

The kidneys are rather large and of nearly equal size. They are surrounded by a large amount of fatty tissue in a condition of serous atrophy. The capsule is not adherent and strips from a smooth surface. The stellate veins are injected. The cortex is swollen, pale and its markings distinct. The pyramids are dark red. The mucous membrane of the pelvis is smooth and free from changes.

The suprarenals are of normal size. The surface is dark in color and studded over with pinhead-sized yellow nodules. The cut surface shows no changes.

The mucous membrane of the stomach is smooth, but is covered by a thick coat of adherent grayish mucus. There are a few areas of submucous ecchymosis.

The mucosa of the large and small intestines is smooth and shows no changes to the naked eye. There is no enlargement of Peyer's patches nor the solitary follicles. A few of Peyer's patches near the cecal valve present the "shaven beard" appearance. The vermiform appendix lies retrocecal and is firmly adherent. Its mucosa is normal in appearance. The mesenteric lymphatic glands are moderately enlarged and firm. They resemble the enlarged glands of other regions.

Several ounces of turbid urine is found in the urinary bladder. The mucosa is smooth and the walls show no changes. Lying in the connective tissue to the left of the bladder is a smooth walled cavity containing an ounce of dark brown fluid. The prostate is not enlarged and on section shows no changes. The seminal vesicles and testicles are normal.

The scalp, skull, brain and its membranes show no changes.

There is no evidence that death was produced by pressure of the enormous glands of the neck or chest upon the trachea, bronchi or great vessels.

Histological Examination.—Pieces of the spleen, liver, lung, kidney, stomach, ileum, colon, suprarenal, tonsil, and the cervical, axillary, and retroperitoneal lymphatic glands were fixed in alcohol containing four per cent. of formalin and sections cut from celloidin in the ordinary way. Sections were stained with hematoxylin and eosin, Van Giessen's method, methylene blue, polychrome methylene blue (alone and with neutral orcein) and with carbol-fuchsin differentiated to show tubercle bacilli.

Lymphatic Glands.—Sections from glands in all the groups examined show practically the same changes.

The capsule is moderately thickened and the cells are some-

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what actively proliferating. The vessels are packed with red blood cells.

The usual picture of lymphatic gland is lost. Cortical and medullary portions can not be distinguished and there are no recognizable remains of the germinal centers. The fibrous stroma is greatly increased and constitutes the larger part of the mass structure.

Under low power are seen irregularly distributed groups of

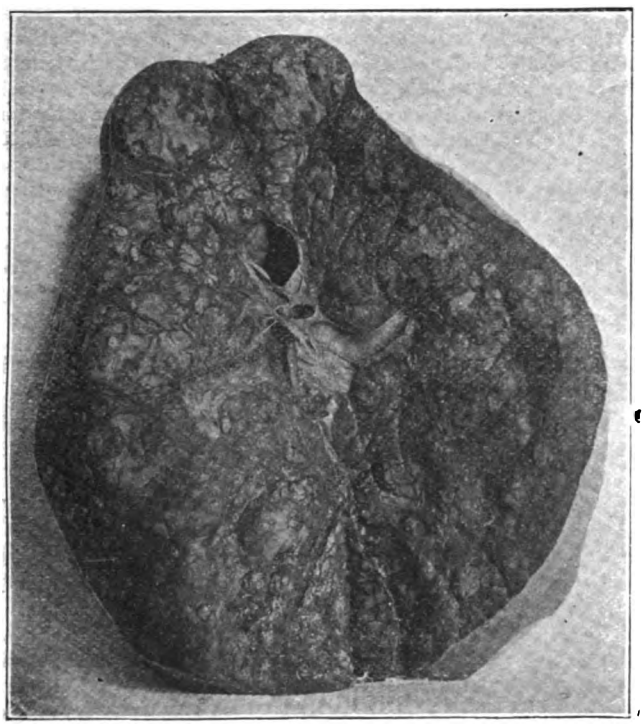

Fig. 2.—The cut surface of the spleen.

closely packed, distinctly staining nuclei. These masses are poorly defined and merge gradually into the fibrous stroma. They have no definite relation to the remaining structure, and have circular, gyrate or no definite outline. In some places there is about an even mixture of connective tissue and distinct nuclei. Rather large, well-filled blood vessels with thick hyalin walls are visible in these areas.

Under high power the masses are seen to be composed of the

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cells one expects to find in a subacute inflammatory process. Mononuclear lymphocytes are present, but their number is greatly exceeded by polymorphonuclears, while the great mass is made up of young proliferating connective tissue cells. Scattered uniformly throughout is a noticeable amount of connective tissue fibers not to be considered "adult." In some areas practically all cells are well preserved; in others the nuclei of the connective tissue have not the usual sharp outline, and are for the most part decidedly granular, suggesting disintegration. This is not so evident in the leucocytes. Moreover, scattered between the cells are minute, deeply staining granules and globules which cause a somewhat blurred field. They are taken to be fragments of nuclear tissue, and furnish further evidence of the karyorrhexis suggested by the granular condition and indefinite outline of the connective tissue nuclei. In still other areas it seems as if the whole mass of cells has undergone this disintegrating process and nothing is seen but an occasional wandering leucocyte.

The connective tissue in places where it predominates is of the adult type, and has for the most part nuclei which stain well. In certain fields, however, the nuclei stain poorly or are entirely absent, the remaining tissue being vacuolated and diffusely granular. Conditions of coagulation necrosis are simulated, and it is often difficult to say how many cells the tissue may have originally contained.

Plasma cells are present, but they have no definite grouping, and are sparsely but diffusely scattered.

Giant cells are also present. They are smaller than the typical tuberculous giant cell and the nuclei are fewer and more densely stained. These are sometimes arranged peripherally but not usually so. They occur chiefly in the more dense cell masses. They are not surrounded by epithelioid cells, and nowhere make up a part of the typical tubercle.

Besides those which are here referred to as giant cells there is another, usually multinuclear cell, which is a conspicuous element of the microscopic picture, both in the densely cellular areas and in those where connective tissue predominates (Figs. 3, 4. 5). They occur most numerously, however, in the latter places. They are not seen in the granular necrotic areas. Typically they have from two to several nuclei (possibly as high as ten) which are characterized by their extremely dense stain with nuclear dyes and their peculiar inter-relations. The stain is so dense that no nuclear structure is visible, except occasionally where there are only two nuclei or a similar cell with a single nucleus. Here a lighter center is sometimes apparent. A uninuclear cell of this type is mentioned because large cells are seen in the same areas whose single nucleus

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stains densely and does not resemble the nuclei of other mononuclear cells present. The binuclear cells have staining properties similar to the mononuclear, and the nuclei are usually concavo-convex with the concave surfaces facing, gonococcus-like (Fig. 3). In those containing more than two the nuclei often have a petiolate arrangement—the individual nuclei roughly triangular and arranged around a common center, one angle of each pointing to the cell center. Occasionally they resemble a knotted cord with communicating processes (Fig. 3). A concentric arrangement around the periphery is occasionally seen, and no sharp dividing line is possible between these cells and those that must be classed as true giant-cells—the differences in form and staining qualities being those of degree rather than of kind. These cells are presumably of endothelial origin.

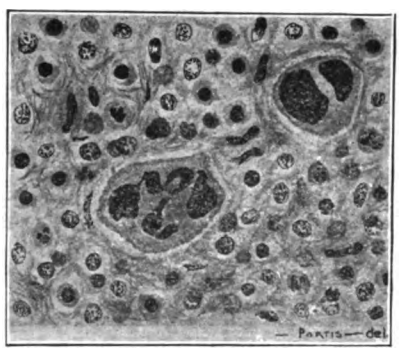

Fig 3.—Section of a lymphatic gland. (Zeiss oil im. $^1/_{12}$, oc. 3.)

Lung.—The alveoli are largely empty; some are filled with a homogeneous substance containing a few pale cells. In places there are dilated or collapsed spaces, and a few are ruptured into adjoining alveoli. The stroma is everywhere rather hypercellular. In certain small areas there are dense collections of deeply staining, small, round cells of the lymphoid type. These cells have mostly single round nuclei, but a few are elongated, irregular or polymorphonuclear. There is considerable perivascular coal pigment and the larger vessels are as a rule filled with red blood cells. The vessel walls are somewhat thickened.

The "lymphoid nodule" is made up of an aggregation of deeply staining cells supported by a connective tissue framework faintly resembling the alveolar arrangement in the lung (Fig. 6). In places the area is sharply marked off from the

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surrounding lung tissue; in others it blends rather freely. The vessels and stroma of this area appear to be those of the original lung substance, and the nodule not to be an entirely new formation. The cells making up the tissue are of various sizes and shapes. Small, round, and oval nuclei predominate, but there are many large, pale cells of the epithelioid type, small lymphocytes, and polymorphonuclear leucocytes. Scattered throughout are many cells containing two to six or eight deeply staining, centrally placed nuclei and having scanty protoplasm. These cells resemble the multinuclear cells of the lymphatic glands, and are presumably identical with them. In places there are granular cells and areas of advanced nuclear fragmentation. A limited amount of coal pigment is scattered throughout. Occupying the center of the nodule is a small cyst which apparently represents the remains of a small

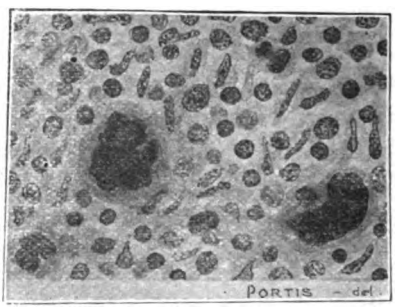

Fig. 4.—Section of lymphatic gland, showing multinuclear large cells. (Zeiss oil im. $^1/_{12}$, oc. 3.)

bronchus. The histology of tubercle is not reproduced, and no giant cells of the tuberculous type are present.

Spleen.—The capsule is universally thickened and shows externally a fibro-granular and in some places an organized fibrous layer rich in young connective tissue cells. The connective tissue stroma is much increased. The vessel walls are irregularly thickened and most vessels are filled with blood cells. Certain areas present a heavy, coarse stroma of mature connective tissue enclosing congested blood spaces. The parenchyma is rather richly cellular. Areas staining deeply with nuclear dyes and made up of fragmented cells are seen which much resemble similar areas in the lymphatic glands. Numerous round or oval areas made up of well-preserved round cells of the lymphoid type with some leucocytes are also present.

The small giant cells are fairly numerous in the better preserved districts, and the very dark staining multinuclear cells

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noted in the glands and lung are irregularly distributed. A greater proportion that must be classed as true giant cells are here present than in the glands, but they differ from those typical of tuberculosis in the same particulars. In a few places the histological tubercle is present (Fig. 7); but in general the structure is but little more suggestive of tuberculosis than is that of the lung or lymphatic glands. The cell areas, either those well preserved or the disintegrated ones, can not be identified as remains or alterations of the Malpighian bodies.

Liver.—The interlobular connective tissue is moderately increased. It is largely of mature type, showing few nuclei In places a mild diffuse interstitial proliferation is seen. Nothing abnormal is noted concerning the bile and blood vessels. For the most part the liver cell nuclei stain clearly and sharply with hematoxylin. In some places, however, they stain faintly and the cells present the appearance of mild cloudy swelling.

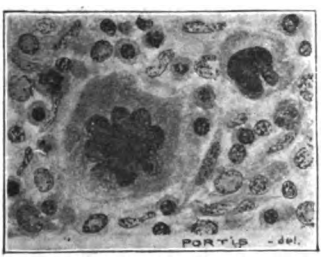

Fig. 5.—Section of lymphatic gland, showing multinuclear large cells. (Zeiss oil Im. $^1/_{12}$, oc. 3.)

This occurs more noticeably in the periphery of the lobules. Throughout a large part of the tissue are scattered oval faint blue granules, the size of cell nuclei, which are taken to be granules of glycogen.

Scattered throughout the parenchyma and its supporting tissue are a limited number of typical tubercles. In the smaller ones typical tuberculous giant cells are centrally placed, and the number of nuclei is sometimes very great. Others contain small caseous areas in the center. The usual endothelial and connective tissue proliferation with numbers of round cells are also found. There are found also some small collections of round cells in the lobules hardly recognizable as tubercles—corresponding to the so-called lymphoid tubercle. The largest tubercles—the bodies styled "lymphoid nodules" in the gross description—are sharply defined from the liver substance, the cells of which are compressed and distorted around

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tue margins and separated from the tuberculous cell masses by a delicate connective tissue structure (Fig. 8). Throughout these tubercles are seen a large number of young blood vessels.

Besides the usual cells making up tubercle, including here small and large typical giant cells, there are seen certain cells of endothelial type with two to five nuclei. There is a sharply-defined nuclear membrane to each, and the interior is clear except for minute points of chromatin. The cell body is relatively small and the protoplasm scanty. They are distinguished from ordinary giant cells by the smaller number, the large size and irregular contour of the nuclei. The stain is often very dark and evenly distributed, and no internal nuclear structure is visible. These cells correspond to those in the

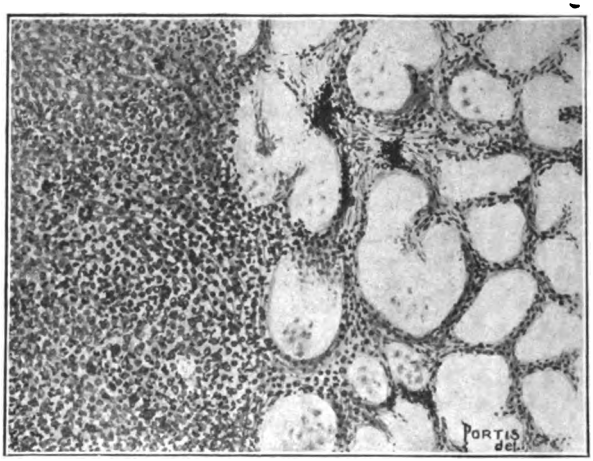

Fig. 6.—The margin of the "lymphoid nodule" in the lung.

lymphatic glands and elsewhere, and the same interrelations of nuclei are noted.

A moderate number of plasma cells are found, particularly in the larger tubercles. They have no definite arrangement or distribution.

Kidney.—The capsule shows no changes. There is a well marked cloudy swelling of the convoluted tubules with slight desquamation. The vessel walls are somewhat thickened. The interstitial connective tissue is slightly increased. Bowman's capsule is, as a rule, visible, but slightly thickened and the nuclei of its lining cells are numerous and prominent. The glomeruli are somewhat shrunken so as not entirely to fill the capsule and the intervening space is partly filled with a vacuolated

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detritus. They are rich in well-stained nuclei. In a single place in the cortex there is a small area so densely filled with small, round mononuclear cells as to obscure the kidney structure. There are to be seen, however, remnants of destroyed tubules. No giant cells are visible. In the immediate neighborhood of this area the epithelial cells show the greatest degeneration noted in any part of the sections.

Small Intestine.—The mucosa is extremely atrophic, being represented only by a low stratum of fibrillated and granular substance densely packed with small, round cells and here and there the remains of a tubular gland. No semblance of villi

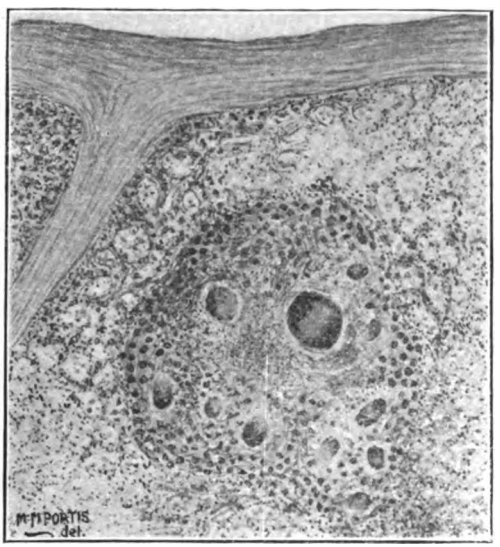

Fig. 7.—A tubercle in the spleen.

remains. The cellular infiltration stops sharply at the submucosa, save in a few places, where there is likewise a round-celled invasion of the submucous tissue. The muscular layer shows little change beyond a hypercellular stroma. The subserous layer is much thickened and the seat of many small collections of round cells, some of which contain central giant cells, and make up the microscopic picture of tubercle. Lying on the serous side of this coat are large, wavy, interlacing strands of a homogeneous material representing the gelatinous exudate on the peritoneum. In places this is invaded by collections of round cells and leucocytes.

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Large Intestine.—There is round celled infiltration of the mucosa, extending in places into the submucosa as small areas. The epithelial structure shows more or less superficial necrosis. The vessel walls are rather thick, and the connective tissue outside the muscular layer shows a condition of mucoid degeneration. The muscle coat is practically unchanged. Tubercles are not seen.

Stomach.—The mucosa is moderately infiltrated with round cells, and there is some epithelial degeneration. The subserous connective tissue is hypercellular, but there are no tubercles. The vessel walls show some thickening.

Suprarenal.—No pathological changes are noted. Separated from the main mass are several small oval areas of adrenal tissue.

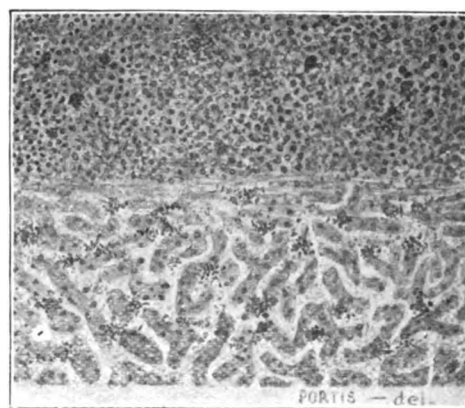

Fig. 8.—The margin of a "lymphoid nodule" in the liver.

Tonsils.—A moderate diffuse cellular hyperplasia is present, but there is no histological evidence of tuberculosis.

BACTERIOLOGICAL EXAMINATION.—Cultures made from the peritoneal fluid gave organisms corresponding in morphology and growth to the staphylococcus pyogenes aureus and albus. In the lung the staphylococcus pyogenes albus alone was found. No growth developed in tubes inoculated from the heart, liver, spleen and lymphatic gland.

Search for Tubercle Bacilli.—Tubercle bacilli, in every way typical, are found to be numerous in the cervical, retroperitoneal and axillary groups of lymphatic glands. They are seen chiefly in the richly cellular areas, lying in clumps and singly, sometimes apparently within but more often between the cells. None were seen in the multinuclear or giant cells.

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In the liver they are found fairly numerous in the solitary tubercles and "lymphoid nodules."

They are found without difficulty in the giant cells and surrounding tissue of the spleen. They are also found in small numbers in the "lymphoid nodule" of the lung.

Many of the subserous tubercles of the small intestine contain large numbers of the organism. A long, rod-shaped bacillus and a large coccus, staining well with methylene blue, are found in the mucosa, but search for the tubercle bacillus here is negative. None are found in the kidney or in the tonsil.

INOCULATION EXPERIMENTS.—Shortly after the autopsy a piece of one of the larger retroperitoneal glands was introduced into the abdominal cavity of a guinea-pig weighing 567 grams. The gland was held in forceps and thoroughly seared in the Bunsen flame. It was then cut open with sterile scissors and a small cube cut from its central portion. This was inserted through an abdominal incision, pushed far away from the opening and the wound closed and sealed. The pig was found dead ten days later, and the body weighed 463 grams.

Postmortem examination revealed the wound sloughing and surrounded by infiltrated tissue. The piece of gland inserted was found deep in the abdomen, just beneath the stomach and adherent to the omentum and mesentery. It presented an appearance almost the same as at the time of inoculation, having undergone no disintegration. It is, however, somewhat more friable and of a more uniformly yellow color on section. The lymphatic glands in the region are slightly enlarged but otherwise unchanged. The abdominal cavity contains a small amount of blood-stained fluid, but there is no visible evidence of peritonitis. The organs do not show changes recognizable to the naked eye.

Histological examination finds the inserted gland necrotic and granular. It fails to take nuclear dyes. About the periphery are many small round cells and leucocytes, which invade the surrounding adherent tissue, including the stomach wall. No histological evidence of tuberculosis is found in the lungs, liver, spleen, kidneys or the mesenteric and retroperitoneal lymphatic glands. Search for tubercle bacilli was not made.

A Gram-staining coccus is found in the peritoneal fluid and an unidentified bacillus in the heart's blood. Cultures from the various organs give no growth.

The animal evidently died from an acute infectious process non-tuberculous in its nature, and without the development of a general tuberculosis.

A second guinea pig, inoculated in the same manner, weighed

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427 grams. It was found dead seventeen days after the operation, and the body weighed at that time 269 grams.

The wound is healed perfectly, and covered by a dry crust. The general peritoneal cavity shows no changes. Extending upward and to the left from the margin of the wound is an intraperitoneal mass, involving by adhesions the margin of the liver, loops of small intestine and the ventral abdominal wall. In the center of this is a small cavity containing thick, yellow pus and the friable and degenerate tissue of the inoculated gland. This abscess lies at the costal arch. The piece of gland retains its original size and shape. The liver contains a mustard-seed-sized yellow nodule in its large right lobe; the lungs are congested and edematous; the other organs are unaltered. The inguinal and axillary glands show a moderate enlargement which is symmetrical. The mesenteric and retroperitoneal glands appear to be normal.

There is no evidence of tuberculosis in the histological appearance of the lungs, liver (the yellow nodule is evidently an old inflammatory focus of questionable nature), spleen, kidneys, or the axillary and inguinal lymphatic glands of the left side.

The piece of gland inserted was sectioned with the stomach, intestine, liver and abdominal wall to which it is adjacent. The gland has become entirely necrotic and appears as a granular mass without nuclei. Its periphery stains deeply from the presence of many polymorphonuclear leucocytes, lymphocytes and nuclear fragments. All surrounding tissue is densely infiltrated with small, round cells, mostly having single nuclei. The adjoining abdominal wall contains a large mass of granulation tissue of varying density, composed mostly of small cells having single nuclei. It contains areas of necrosis and of nuclear fragmentation much resembling the structure of the original lymphatic gland. No giant cells or histological tubercles are found. Search for tubercle bacilli in this tissue gives negative results, but immense numbers of a small coccus, singly and in colonies, are found.

Here again it is evident that the animal died of an acute infectious process without the development of a general tuberculosis.

SUMMARY: Briefly stated the findings in this case are:

1. Symmetrical hyperplastic lymphadenitis, of slow development and chronic course, beginning in the right cervical region, attended by enlargement of the spleen, slight irregular temperature, and general emaciation.

2. Clinical diagnosis of pseudoleukemia.

3. Moderate secondary anemia with a terminal leucocytosis of 19,000.

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4. Termination by extensive peritoneal and visceral tuberculosis and final infection with the staphylococcus pyogenes aureus.

5. Postmortem anatomical diagnosis of pseudoleukemia with enlargement of the cervical, axillary, mediastinal, peribronchial and retroperitoneal groups of glands, lymphoid nodules in the liver, spleen and lungs, fibrino-plastic peritonitis; no evidence of old or recent tuberculosis in the lungs.

6. Histologically, fibrous and cellular hyperplasia of the lymph glands and the spleen, with areas of necrosis; tubercles in the liver, spleen, kidneys and peritoneum.

7. Tubercle bacilli in the lymphatic glands, spleen, peritoneum and in the lymphoid nodules of the liver and lungs; staphylococcus pyogenes aureus and albus in the peritoneal fluid and albus in the lung.

8. Inoculation of pieces of the lymphatic glands into the peritoneal cavity of guinea-pigs not positive of tuberculosis; death from suppurative lesions after ten and seventeen days respectively.

In the clinical and postmortem findings of this case a picture is presented which seems to fully warrant the conclusion at first drawn, namely, that it was a case of pseudoleukemia. The peritonitis does not belong among the anatomical findings of that disease, but it may be looked upon as a secondary or terminal process. The condition of the spleen was, perhaps, what should arouse a suspicion that a chronic tuberculous process was present. Such a suspicion was aroused at the time of the autopsy, and investigations were carried out to the end of determining that point. Yet while such gross anatomical lesions as those found in the spleen might have indicated a localized tuberculosis, it was left to microscopical and bacteriological examinations to reveal the existence of well-established general tuberculosis in the lymphatic and visceral lesions so plainly pointing to pseudoleukemia. The anatomical findings are certainly not those of the ordinary form of tuberculous lymphadenitis.

It is disappointing that the inoculation experiments added so little confirmatory evidence to the presence of tubercle bacilli in the affected glands. Fortunately such

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evidence is in this case unnecessary. The failure of the inoculations to furnish it is to be explained by the poor technique of the operations. It is to be remembered that a single large piece of the gland was inoculated into the peritoneum in each case and that this piece of gland was found practically intact upon the death of the animal. It had undergone necrosis, but had not become disintegrated. Had the tissue been finely divided before inoculating, there can be little doubt but that the result would have been different.

It is easy to understand how in such a chronic wasting disease, with decreasing physiological resistance to infection, a tuberculosis might be added to an already existing Hodgkin's disease, thus making a complex and complicated anatomical condition. In the light of the completed findings, however, the interpretation of this case must be made upon a different basis.

There was not found either an old or recent tuberculosis in the lungs or the intestines, or in any part directly accessible to external infection, by which to explain the entrance of large numbers of tubercle bacilli into the blood or lymph streams and their general distribution. And if in some unknown way such an entrance of bacilli had taken place, why should their distribution to the already diseased lymphatic glands and lymphoid nodules be universal and practically all other parts be spared? It is more reasonable to suppose that tuberculosis of the glands of the right side of the neck was the primary affection. Although the microscopic examination does not show the ordinary picture of such a condition, the findings are as easily explained upon that basis as upon any with which we are familiar; and the finding of tubercle bacilli in tissues showing undoubtedly a chronic inflammation (fibrous hyperplasia and multinuclear cells) is strong presumptive evidence that they had much to do with the lesions. From this primary group the other groups became secondarily involved; and these also be-

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came old lesions before the final rapid spread in the peritoneum and liver and the terminal staphylococcus infection determined the fatal issue.

In the same class with this belong a number of cases reported in the literature, under various titles, usually as combinations of pseudoleukemia or lymphosarcoma and tuberculosis, sometimes as tuberculous lymphadenitis simulating pseudoleukemia. They are cases presenting the symptom complex and postmortem findings of Hodgkin's disease, tuberculosis being first demonstrated by the microscopic examination or by animal inoculation. Sternberg[32] has recently brought together the scattered literature of the subject in a critical review, and a part of what directly follows is based upon his article.

There is nothing characteristic in the gross appearance of the glands of such cases. They are large, firm and as a rule sharply outlined from the surrounding connective tissue. On the cut surface they vary in color from gray to yellow and often show small spots which present themselves to the naked eye as areas of necrosis or even of caseation. So far we are not able to say that such areas are positive evidence of tuberculosis or that their absence indicates that the disease is non-tuberculous. In the liver, spleen and other viscera there are found nodules resembling in every way those of ordinary pseudoleukemia. Acute tuberculosis of some part of the body may be found as a terminal process.

The microscope does not of necessity reveal the tubercle. The connective tissue is moderately increased and there are likely to be found areas of necrosis or nests of large pale cells rich in protoplasm and bearing one or more deeply staining nuclei. True giant cells may be found, but the familiar picture of tuberculosis in its ordinary form is absent and it may be impossible by the microscope alone to determine that the disease is present.

In an earlier article Sternberg[31] has insisted upon the constant presence of a large cell of endothelial origin

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containing one to six nuclei, with abundant protoplasm and occasionally containing karyokinetic figures which stain deeply. They are not identical with the epithelioid cell, are not found in normal organs nor in glands the seat of pseudoleukemic changes, and are considered characteristic and diagnostic of tuberculosis. Multinuclear cells were found in my examination of the lymphatic glands, the spleen, the liver and the lung, which possibly correspond to these cells; but they are not distinctive enough, nor is Sternberg's description of the histology and reactions of his cells characteristic enough to assign to them absolute diagnostic importance in the absence of demonstrable tubercle bacilli or histological tubercles. They correspond in a general way to cells of endothelial origin occurring in the course of chronic inflammation in various parts of the body, as described by other writers. Freiherr von Notthaft[13] describes endothelial proliferation, with the formation of cells containing up to ten nuclei, in what is otherwise a pure lymphosarcoma, metastases in the skin being free from such cells. He calls attention to similar findings by Langhans, Ribbert, Dreschfeld and Boetcher.

Goldmann[17] has insisted that in glandular hyperplasias of indefinite histological character the presence of eosinophiles in any considerable number speaks against tuberculosis. In typical histological malignant lymphoma he found them to be very numerous. Kanter,[20] pursuing the work of Goldmann, found that in tuberculous processes of similar microscopic appearance the number of eosinophiles varies greatly. Dietrich[10] concluded that eosinophiles are of value in excluding tuberculosis, while Fischer[12] and other observers reach an opposite conclusion.

According to Sternberg[32] the first case belonging to this group is reported by Wunderlich (*Arch. de Heilkunde,* 1866). He found hyperplasia of many lymphatic glands, some of which had caseous areas, a spleen of

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twice the normal size and containing lymphoid nodules, two caseous nodules in the brain and several small yellow tubercles in the kidneys. Among the older cases is also probably that of a hard lymphosarcoma with giant cells reported by Langhans (*Virch. Arch.*, 54, p. 509).

Cases presented to the London Pathological Society by Murchison,[24] Dickinson[9] and others probably belong here, but lack of completeness in the reports renders a decision at this late day arbitrary and valueless.

Delafield[8] describes a case of acute tuberculous lymphadenitis of almost universal distribution, simulating malignant lymphoma clinically, and refers to similar cases of Hilton Fagge and Pye Smith.

Askanazy[1] records a case of tuberculosis of the supraclavicular, bronchial and mesenteric glands, without involvement of the lungs or intestines, which gave the clinical picture of malignant lymphoma and was called pseudoleukemia by Baumgarten at the autopsy. The description of the glands corresponds closely to those in the case here reported and only the microscopic examination discovered the presence of tuberculosis by demonstrating the bacillus. The case was considered one of combination of the two diseases.

Waetzoldt[37] made a clinical diagnosis of pseudoleukemia in a case which showed at the postmortem examination enlargement of the lymph glands and spleen and pinhead-sized white nodules scattered diffusely throughout the lungs. The retroperitoneal, mesenteric, mediastinal and bronchial glands were large, firm and discrete and did not show areas of caseation. There were no old tuberculous lesions in the lungs or elsewhere. Microscopic examination revealed many tubercle bacilli in the lungs and mesenteric glands, but none in the glands surrounding the bronchi. There were no structures histologically recognizable as tubercle. The author inclined to the belief of double infection.

Brauneck[3] records a case in which the autopsy re-

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vealed a large group of caseated glands pressing upon the common bile duct giving rise clinically to grave icterus. There was enlargement of the spleen with hyperplasia of its follicles; many small yellowish nodules were found under the capsule of the liver, and the retroperitoneal supraclavicular and cervical glands were caseated without enlargement. He considered the case one of pseudoleukemia. Sternberg[32] believes that the deduction is not warranted and that the changes were of a tuberculous nature, which seems by far the more probable explanation.

A case presenting great enlargement of the submaxillary, supraclavicular, axillary, and inguinal glands was diagnosed clinically as pseudoleukemia by Brentano and Tangl.[4] There was no clinical evidence of tuberculosis in the lungs or elsewhere. Late in life a bronchial catarrh developed, but the sputum did not contain tubercle bacilli. At the autopsy there were found areas of healed tuberculosis at the apices without enlargement of the bronchial glands. The enlarged glands of other regions showed no gross or histological evidence of tubercle, and search for the bacilli was negative. Nevertheless, guinea-pigs inoculated with pieces of the glands died of typical inoculation tuberculosis and the authors do not hesitate to conclude that such was the original nature of the disease.

Reinert[27] speaks of a case of widely distributed lymphoma of the neck, mediastinum, and mesentery with lymphoid nodules in the lung and liver and hypertrophy of the spleen. The anatomico-pathological diagnosis by Baumgarten was pseudoleukemia. Tubercle bacilli were found in all the glands searched and these were considered the original cause and explanation.

Here also belongs a case of Weisshaupt's.[38] The autopsy diagnosis was pseudoleukemia, while the microscope revealed a rare form of lymph gland tuberculosis without caseation, but with areas of coagulation necrosis.

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He says that such a form of necrosis speaks in favor of tuberculosis against other forms of glandular hyperplasia and that the diagnosis of pseudoleukemia is to be considered absolute only when tuberculosis is carefully excluded by microscopic examination. In an examination of twelve cases from spirit preparations he found no areas of necrosis and no tubercle bacilli.

A case of tuberculous disease of the cervical, axillary, inguinal, and abdominal lymph glands resembling Hodgkin's disease is referred to by Bramwell[2] in his recent work on "Anemia."

Courmont, Tixier, and Bonnet[6] have recently furnished a detailed report with experimental investigation of a case of generalized lymphatic tuberculosis corresponding accurately to the clinical type of Hodgkin's disease. They have given also a valuable consideration of the general pathology and pathological relations of lymph gland tuberculosis.

Sternberg[31] examined eighteen cases that appeared clinically and anatomically as pseudoleukemia and found fifteen of them to be tuberculosis. He concluded that the greater number of all cases diagnosticated as Hodgkin's disease would be proved to be tuberculous lymphadenitis if properly analyzed.

Troje,[34] Cordua,[5] Ricker,[29] Dietrich,[10] Fischer,[12] Jacusiel,[19] Freundweiler,[14] and Czerny[7] have recorded cases which belong to this class and which show the various characteristic findings in a more or less typical way.

Cases have been now and then observed showing the symptoms complex and anatomical findings of typical pseudoleukemia to which is added recurring periods of fever varying in duration from eight to fifteen days. Sternberg[32] believes that the majority of these are of tuberculous origin, though other causes are to be assigned to some of them. Ebstein[11] first called attention to the condition in 1887, and cases are reported by

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Pel,[25 26] Klein,[21] Völkers,[36] Renvers,[28] Hanser,[16] and others.

Concerning the explanation of the facts in such cases as have been noted in the foregoing, the different authors have held varied and somewhat contradictory opinions. Some, while admitting the existence of a tuberculous infection, have been inclined to look upon it as an entirely secondary and complicating condition and in no way concerned in the primary etiology. Such a conclusion is reached by Askanazy,[1] Wetzhold,[37] Fischer,[12] Troje,[34] Claus (ref. by Courmont), Cordua[5] and Lichtheim.[22]

A certain number of cases must no doubt be so explained. The adverse influence of any wasting disease, lessening the power of resistance to infection, may allow of the development of tuberculosis where it would otherwise not appear; and there could be no greater fallacy than to conclude that wherever the tubercle bacillus is found it is the cause of all the clinical and anatomical phenomena presented.

In a recent contribution Gilbert and Weil[15] insist upon the frequency of secondary tuberculous infection of glands the seat of malignant processes. They report a case of lymphosarcoma developing in the inguinal and abdominal glands of a patient affected by an old tuberculous pleurisy. An excised gland did not show the microscopic changes characteristic of tuberculosis, but when introduced into guinea-pigs gave rise to typical inoculation tuberculosis of rather slow development. They take issue with the conclusions of Brentano and Tangl,[4] Ricker,[29] and others and insist that such cases as show lymphosarcoma histologically, even though containing demonstrable tubercle bacilli, are secondarily infected.

Most of the authors look upon the organism in such cases as the primary etiological factor and the disease as a tuberculous lymphadenitis simulating pseudoleukemia, pointing out the necessity of animal inoculation in the establishment of a diagnosis. But, while maintaining

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that the tubercle bacillus is the cause of the greater number of cases of so-called Hodgkin's disease, Sternberg,[31 32] draws a sharp line of distinction between the two conditions. Dietrich[10] shares his opinion in part and Ricker[29] goes so far as to attribute the development of a true lymphosarcoma to the presence of a previous tuberculous infection.

Courmont, Tixier, and Bonnet[6] insist that such cases constitute a special form of pseudoleukemia—a disease giving rise to a somewhat definite group of clinical and anatomical phenomena, but assignable to different causes. Sabrazés (quoted by Courmont, Tixier and Bonnet) and Delbet (*ibid.*) also isolate a tuberculous type of the disease and the infectious origin of Hodgkin's disease is strongly maintained by Bard (*ibid.*). Cadiac (*ibid.*) calls attention to a similar disease occurring in the horse, dog, cat and cow, and says that it is not a special malady but a syndrome produced by various infectious agents, foremost among which is the tubercle bacillus.

Other authors have explained certain cases of Hodgkin's disease as due to definite organisms. Verdelli (quoted by Stengel, *Twentieth Century Practice,* 1896, vii, 446) found bacteriological research positive in twenty-nine cases. Majocci and Piccini (*ibid.*) demonstrated bacilli and streptococci; Klein (*ibid.*) found micrococci; Mafucci (*ibid.*) streptococci; Roux and Lannois (*ibid.*) found a variety of staphylococcus pyogenes aureus which produced glandular swelling in inoculated animals. Delbet (*ibid.*) cultivated a bacillus from the spleen which produced glandular swellings when introduced into animals, and one from the glands of a woman which produced emaciation and enlargement of the glands in a dog. The same organism was recovered in culture and was thought to be the cause of the disease.

Murray,[23] writing for Allbutt's "System of Medicine," says: "When we consider the many points of analogy between Hodgkin's disease and tuberculosis and

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the other infective processes, it seems very probable that Hodgkin's disease is also due to infection. The changes which we find in the lymph glands are most easily explained by assuming that they are the result of some pathological parasite."

Strümpell[33] says that it is lately shown that Hodgkin's disease belongs to the class of infectious diseases and that many cases seem to go back to tuberculosis—to be purely tuberculous lymphadenitis without infection of other parts, but adds: "It is still questionable if this accounts for all cases of pseudoleukemia," thus at least giving recognition to the question.

Since the histology of pseudoleukemic glands in the ordinary form is practically that of small round-celled sarcoma it is well to add here a recent statement in *Progressive Medicine*:[18] "It may be said that malignant tumors, especially those now classed as sarcoma, very probably include peculiar proliferative processes caused by organisms whose exact nature has not yet been determined. The near future will undoubtedly witness the definite separation from the sarcomas of various distinct infectious growths, and it would not be surprising if in the end a large number of sarcomas were to resolve themselves into processes of parasitic origin. As is frequently remarked, sarcoma in its clinical and anatomical characteristics presents more and more marked analogies to chronic granulomatous processes than carcinoma. This is especially true of small-celled forms."

So far investigation does not warrant us in concluding that all pseudoleukemias are even probably tuberculous in origin, but it is at least established that tuberculous lymphadenitis may give rise to the symptom complex and anatomical findings which furnish thus far the only basis for the recognition of that disease as a distinct entity.

Already enough fairly typical examples have been pre-

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sented to prove that it is not an altogether infrequent condition; and in the more complete analysis of future investigation it will in all probability be shown to be more frequent than at present indicated.

The great number of names which have been applied to the condition here designated as pseudoleukemia, based upon the somewhat varied clinical course as well as a limited variation in the gross and minute pathological changes, and the greatly differing interpretation of those changes by different observers, are evidence of the heterogeneity of the class to which the name refers. The etiology is for the most part admittedly unknown; it is also admittedly various. Symptom complex determines the disease as the disease is now understood. Why, then, exclude those cases in which the tubercle bacillus is known to be the cause? A case of known origin is not to be singled out and classed as a different disease, but as an etiological subdivision of the heterogeneous class.

A tuberculous lymphadenitis developing in the guise of pseudoleukemia is, so far as the significance of our present nomenclature goes, a tuberculous pseudoleukemia. So much the more is this term applicable since the histology of such a tuberculosis is frequently only that of ordinary lymphoma, inoculation of susceptible animals often furnishing the only evidence upon which correct diagnosis is possible.

I am indebted to Professor Senn for the privilege of using the case herewith presented, to Professor Hektoen for advice and counsel in the preparation of this report, and to Mr. M. M. Portis for the drawings.

November 13, 1899.

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PRIMARY SARCOMA OF THE SPLEEN.*

ELLSWORTH D. WHITING.

Male, laborer, aged 30, Swede, admitted into the Cook County Hospital Dec. 6, 1896, and died Dec. 16, 1896, from general peritonitis following appendicitis. A laparotomy was performed five days before death.

The postmortem examination was held twenty-four hours after death (Dr. Hektoen).

Anatomical Diagnosis.—Diffuse purulo-fibrino-hemorrhagic peritonitis; chronic appendicitis; laparotomy; cloudy swelling of kidneys; lobular pneumonia; arteriosclerosis of aorta; chronic gastritis; scoliosis; sarcoma of spleen.

The body is well nourished, fully developed and mus-

* The specimen and notes of this case were presented by Dr. Hektoen in the name of the late Dr. Whiting. Dr. Whiting was an interne in the Presbyterion Hospital, and died at the threshhold of a most promising career. He had intended to make a complete study, literary and otherwise, of sarcoma of the spleen.

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cular; postmortem lividity posteriorly; rigor mortis marked; thorax oval; abdomen distended. Above and parallel with Poupart's ligament, on the right side, is an operation incision 10 centimeters in length and drained at its lower extremity by a piece of gauze.

The abdominal cavity contains a small amount of reddish, turbid fluid. The large and small intestines are distended, deeply injected, covered with fibrinous exudate and matted together by fibrinous adhesions. The parietal peritoneum is congested, hemorrhagic in areas and covered with fibrinous exudate.

The appendix is 6 centimeters in length and bound to the cecum by adhesions which hem in a pocket of pus. The glands about the appendix are enlarged.

The pleural cavities are empty and the pleuræ are smooth.

The left lung and upper and middle lobes of the right lung are edematous. The inferior half of the lower right lobe contains dark red, solid masses which sink in water. The bronchioles in this portion are filled with casts.

The pericardium is empty and its layers smooth.

The heart weighs 440 grams. The valvular endocardium is smooth; the coronary arteries are normal; the myocardium firm, shining and oily. The left ventricle is from 1 to 1.5 centimeters in thickness and 8 centimeters in depth.

The ascending aorta presents few yellow areas. Similar areas are found in the descending aorta, which is covered with reddish granular, adherent, thrombotic masses. The intima of the abdominal aorta is smooth and non-adherent; clots fill the outgoing arteries.

The mucous membrane of the tongue, nares, pharynx, trachea and esophagus is smooth and covered with a yellow shiny fluid. The mucous membrane of the fundus of the stomach is thrown into heavy folds and covered by a slaty mucus, the remaining surface being of a yellow color. The mucous membrane of the large

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and small intestines is deeply injected, especially in the region of the ileo-cecal valve. A muco-purulent fluid issues from the opening between the cecum and appendix. The mucous membrane of the appendix is greatly thickened; its lumen greatly diminished in size and contains pus. No perforation is present.

Lympho-sarcoma of spleen.

The liver weighs 2000 grams; is soft, and the lobular markings are distinct.

The gall-bladder is free and contains no calculi.

The spleen weighs 300 grams. In length it is 16.5 centimeters; in width 8.2 at a distance of 4.6 centimeters above the inferior margin, and 10.1 centimeters at a distance of 4.6 centimeters below the upper margin.

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The inferior portion is 1.9 centimeters in thickness and the superior 4.6 centimeters. The capsule is slightly thickened, being thrown into folds below, and is smooth and tense above. The lower portion of the organ is firm in consistency and normal in color. The upper portion presents a prominent spherical enlargement which involves the entire region. Its consistency is firm yet elastic; it is normal in color except in irregularly circular areas varying in size from a millet seed to a silver half-dollar where the color is grayish white. To the anterior surface of the tumor is attached a portion of omentum. A shallow, clear-cut notch is present upon the anterior margin.

Upon section the inferior portion of the spleen is reddish brown in color and a slight increase in connective tissue is apparent. The upper portion shows a prominent, distinctly defined, circular, firm, grayish white, bulging, lobulated mass. The lobules vary in size from a grain of wheat to a hazelnut. They are readily detached and seem to be separated from one another by narrow bands of connective tissue. The mass is surrounded by a thin layer of apparently normal splenic tissue. However, at certain points, the mass reaches the surface, where it is in direct contact with the capsule. These points correspond to the light areas observed externally. Few hemorrhagic foci are present. The entire growth is readily enucleated from the surrounding splenic tissue. The attached omentum presents no change.

The kidneys weigh 300 grams; are soft in consistency and yellowish gray in color. The capsule is adherent in places. Section reveals much blood. The cortex is yellowish gray, opaque, and its markings are distinct.

The bladder, prostate gland, seminal vesicles, pancreas, brain and spinal cord show no pathologic changes.

The spine presents a slight left scoliosis in the upper lumbar region. On section the vertebræ are normal.

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The microscopic examination of the tumor of the spleen shows very small round cells diffusely infiltrated in a rather granular, at times more homogeneous, fibrous stroma. The structure corresponds well to that of the so-called lymphosarcoma.

May 14, 1900.

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THE SKIN.

OÏDIOMYCOSIS (BLASTOMYCOSIS) OF THE SKIN AND ITS ORGANISMS.*

HOWARD T. RICKETTS.

Through fortunate associations with Professors Hyde and Montgomery in their clinical work at Rush College and elsewhere, and with Professor Hektoen in the Rush Pathological Laboratory during the past two years, I have been able to study the clinical, histological and mycological features of an unusual number of cases of so-called blastomycetic dermatitis. Of these, six occurred in the private and clinical practice of Professors Hyde and Montgomery, one came to my dispensary clinic at Rush, two were found among old specimens in the pathological laboratory (one by Professor Hektoen and one by Dr. Le Count), and two I obtained from outside sources.

Seven of these cases have yielded cultures of organisms which are considered to play the etiological rôle; these are now growing in pure cultures. Two other cases also yielded organisms which, for unknown reasons, did not live into the second generation; hence they received little morphological and no pathogenetic study.

About forty animals have been inoculated with four of the organisms; the pathogenic properties of the remaining three have not yet been ascertained.

Although the histopathology and mycology are the

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* A full report of this work appears in the Journal of Medical Research, 1901, vi, 377-547.

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features of immediate interest to-night, it is pertinent to consider briefly the clinical type or types of the disease.

In all cases the first noticeable lesion is a small papule, which soon becomes a pustular and later a suppurating and crusted focus. Ulceration extends peripherally, and in three to six weeks the surface shows a beginning verrucous or papillomatous condition. In two to four or six months it reaches a diameter of from one to two and a half inches, the periphery becomes more markedly verrucous and the center depressed; the latter may lose its verrucous structure entirely and be occupied by suppurating and exuberant granulation tissue. The periphery is surrounded by an areola of red or livid unbroken skin, beneath the horny covering of which are seen, typically, many small yellowish points—minute abscesses.

As still further extension occurs the peripheral verrucous tissue becomes more gross, certain papillæ may give off secondary processes and the whole mass overhang the surrounding areola, cauliflower-like. Likewise the central flattening increases, and healing and dry epidermization may take place. Thus, as peripheral extension proceeds, central healing occurs, with marked cicatrization.

Because of the small number of cases observed it would be imprudent to draw positive conclusions concerning different clinical types of the disease. If differentiation can be made at present, it depends on the amount and gross nature of the papillæ, and the number of miliary abscesses in the areola. Certain cases show these conditions in an extreme degree (the specimen exhibited to-night being an example); others have smaller papillæ and a smaller inflammatory areola which contains fewer or no abscesses. It is not improbable that these differences depend purely on variations in the virulence of the infections. However, they are

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associated with other conditions (histological and mycological) which will be referred to later.

Untreated, or improperly treated, the disease may continue for many years, leaving cicatricial deformities; there may be complete spontaneous recovery, or, there is reason to believe, the patient may die of metastatic pulmonary or general invasion by the fungus. It seems probable that under internal administration of the iodid of potassium, in sufficiently large doses, the process, when limited to the skin, will resolve completely in all cases, leaving only the necessary cicatricial deformity. So far it has not been possible to ascertain the value of the remedy in the generalized infection.

I present for your inspection to-night an example of the gross tissue appearance in man, slides showing histological changes, cultures of three types of the organism, and animal tissues illustrating in part the results of experimental inoculations.

The human tissue, representing two years' duration of the infection, shows typically the peripheral, exuberant, cauliflower-like, papillomatous tissue, and the central depressed, cicatrizing area described above. A cross-section of the entire specimen allows the naked eye recognition of three anatomo-pathologic zones: 1, the surface papillary zone, composed of papillæ which rise above the surface level, adjacent papillæ being separated by well-marked clefts or spaces, which in a fresh state are filled with pus; 2, the deep papillary zone, composed of the downward continuation of the surface papillæ, the individuals here being closely cemented to neighboring papillæ by their horny sheaths, and each containing a vascularized "core;" 3, a deeper homogeneous, densely cellular, rather soft, grayish-red zone, which may contain small hemorrhages and minute abscesses; it measures from two to three millimeters to a centimeter in thickness. The tissue immediately underlying

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is the subcutaneous fatty layer, which, apart from some unusual vascularity, appears normal.

Histopathology.—There are few new points in minute structure to be added to those already described, particularly by Gilchrist and Hektoen.

The epithelial hyperplasia is so great and of such a character that Hektoen called it *carcinomatoid,* and Coates, in his case, considered the histological structure typical of epithelioma. Corresponding to the naked eye observation, the epithelial tissue microscopically is seen both to rise above the general level and to penetrate the underlying cellular tissue. The superficial finger-like processes are epithelial shafts, each possessing a slender vascular papilla. Each has a thin horny sheath, which covers the mass of large edematous cells of the rete mucosum. Masses of desquamated and imperfectly cornified horny material lie in the interpapillary clefts, where they are infiltrated and surrounded by leucocytes and ordinary bacteria. A stratum lucidum appears to be always absent, and the granular layer is present inconstantly. When the latter is entirely absent, cornification proceeds no farther than mere flattening of the overlying cells and their nuclei. Examples of imperfect cornification are found also in the deep parts of the rete, in single cells or small groups of cells, and around points of inflammatory reaction (giant cells, leucocytic accumulations and intra-epithelial abscesses. Such cornification may take place with or without the intervention of kerato-hyalin; in the latter case the result being a wider departure from normal horny tissue than in the former. Single cells appear never to be completely cornified; they assume a nearly spherical shape, lose their prickles, the protoplasm becomes rather dense and strongly acidophilic, usually containing no kerato-hyalin, and the nucleus may be shrunken and retracted, leaving a clear, irregular, perinuclear space. Such a cell may be phagocytic, or undergo cell invasion by another

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epithelial cell, or by one or more leucocytes, or both; often it is surrounded by a number of leucocytes. This type of cornification is not often confined to one cell, however; very early, adjacent cells become somewhat flattened and more acidophilic, a few kerato-hyalin granules are evolved, the prickles lost, and an incipient epithelial whorl or pearl thus instituted. The center of such a mass is usually occupied by a few polymorphonuclear leucocytes (and eosinophiles in some cases), occasionally by one or two multinuclear giant cells, or by one or more fungous cells. The innermost epithelial cells may become flattened and granular, may be desquamated, and, as larger numbers of leucocytes penetrate to the center, constitute a part of the contents of an intra-epithelial abscess. The whorls almost never reach the degree of cornification seen in some epitheliomas. It is common to find a thin zone of flattened, partly cornified cells, as the wall of an intra-epithelial abscess. Another condition is found which it seems proper to interpret as an elementary stage of cornification; the prickles of mucosal cells which are adjacent to giant cells, abscesses or a group of organisms, may be transformed into a dense, homogeneous, acidophilic fiber which unites adjacent cells closely. Where a rather large area is involved the change results in a net-like appearance of the field. More remote from the center of reaction prickle-formation obtains again.

The deep contour of the epithelium is various and grotesque, from the presence of bulky masses or delicate finger-like processes, which are always continuous with the surface epithelium, i. e., there are no isolated epithelial nests in the corium. A columnar basal layer, with deeply staining nuclei and mitoses, is always present, the cells undergoing lateral elongation when the processes are drawn out and fiber-like. The hyperplastic pegs may reach the full depth of the underlying cell

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infiltrate, but they never penetrate the adipose or muscular tissue. Areas of atypical cornification and intra-epithelial abscesses are found chiefly in this portion of the epidermis.

Wells noted the presence of multinuclear giant cells in the intra-epithelial abscesses and stated the alternatives, that they must have formed either from the epithelial cells or from cells which had wandered into the epithelial layer (leucocytes). The number of such giant cells varies in different cases. They are found in the intra-epithelial abscesses of all cases, and in addition are usually to be seen in the body of the rete, unassociated with veritable abscesses. In sections shown to-night it is possible to trace their formation from the epithelial cells of the rete. The first step consists of the presence of foreign cells, such as several leucocytes or one or more organisms. Following this, the nuclei of adjacent epithelial cells become smaller and stain more deeply; the prickles gradually disappear, the cell bodies become smaller and by fusion constitute a multinuclear giant cell, the nuclei of which are disposed peripherally. Although mitoses may occur in this process, it has not been possible to find them. A further accumulation of leucocytes leads to the formation of a small abscess; and so it happens that in most intra-epithelial abscesses there are one or more giant cells which possess epithelioid nuclei, and which may contain one or more leucocytes, or organisms, or both.

Intra-epithelial abscesses vary in size up to a millimeter or more in diameter. In their genesis leucocytes seem attracted to certain points by the presence of fungous cells. While the polymorphonuclear always predominates, eosinophiles are present in rather large numbers in cases caused by the mold type of the fungus. Rarely a plasma or a mast cell is seen in this situation and there may be numbers of red blood cells. The presence of giant cells has been mentioned. Protoplas-

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mic granules and nuclear detritus result from the disintegration of leucocytes and desquamated epithelial cells. The parasite in varying numbers, and often in a budding state, is found in the abscesses.

Curious changes are noted in epithelial cells which lie free in the abscesses, having been shed from the abscess wall. Some are long, delicate fibers containing a needle-shaped nucleus, the cell body staining deeply with eosin. Others become perfectly spherical and partly cornified. Still others are phagocytic and may include many leucocytes or other epithelial cells to such an extent that only a thin film of the phagocytic cell remains to surround the enclosed mass. It seems very probable that cells undergoing similar changes have been called parasites when seen in carcinoma.

In addition to abscess formation, polymorphonuclear leucocytes may infiltrate the rete diffusively, and in those cases from which a mold fungus has been cultivated, eosinophiles have a similar distribution, although in fewer numbers. The parasite is occasionally found between epithelial cells, unassociated with leucocytic accumulations.

The corium shows marked edema, small abscesses, diffuse infiltration with wandering cells, tubercles containing giant cells, proliferation of fixed elements and vascular dilation. The subcutaneous abscesses are not so sharply defined as those in the epithelium, and contain, besides the leucocytes, giant cells, portions of connective tissue, blood and the organisms. Plasma cells occur in dense numbers everywhere, except in and immediately around abscesses. They appear to be indirectly associated with the formation of a peripheral, protective zone of fibrous tissue. Russel's fuchsin bodies often may be demonstrated in them, or in intercellular spaces. The tubercles and giant cells resemble closely those seen in tuberculosis. Central necrosis, however, is either absent or inconspicuous. Those cases

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from which the mold type of the organism has been cultivated, constantly show large numbers of eosinophiles; they are found in the granulation tissue and abscesses of the corium and, as mentioned, in the rete mucosum, in smaller numbers.

Mast cells have multiplied greatly and are distributed moderately among plasma cells and areolar and muscular framework; they are grouped particularly, however, about hair follicles and sweat and sebaceous glands.

Whatever the variations in the cultural appearance of the organisms, their morphology in human tissue is nearly uniform. As stated, they occur in the epithelium and corium, commonly in abscesses but often free in the epithelium, or granulation tissue of the corium. They exist singly, in pairs or in small groups, which form conspicuously in certain cases. There is little to add to Gilchrist's description of their form in tissue. The size varies from 8 to 14 microns. Uniformly one finds a doubly-contoured capsule and a central protoplasm which may be vacuolated or may contain a number of spore-like bodies, and which is, moreover, finely reticulated. The affinity of the protoplasm for nuclear dyes varies; sometimes it stains faintly or not at all, and again so deeply that no structure is discernible. Quite constantly a clear zone is found between the capsule and protoplasm; its structural nature is not clear. In certain cases an irregular laminated layer surrounds the capsule of the organism. Busse, Curtis and Gilchrist have also mentioned this structure, Busse calling it an adventitious or accidental capsule. Its origin probably lies in a chemical action of the organism on surrounding tissue fluid. Budding is the only clear method of proliferation in the parasitic state. It is not improbable that endogenous spores form also, but satisfactory proof has not been found. True hyphæ do not form in tissue.

Cultures.—Pure cultures are obtained most readily

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from the small abscesses in the areolar skin after the surface is cleansed with an antiseptic. Inoculations from the verrucous surface tissue result in mixed cultures. Tissue may be disintegrated in a sterile mortar containing one or two c.c. of bouillon, and the resulting suspension made into agar plate cultures; mixed growths are very likely to occur, however. Ordinary media may be used, but a saccharine, faintly acid medium seems preferable. Certain organisms (the mold fungi) could be grown at first only on the maltose-agar preparation of Sabouraud. They all grow readily at room temperature and rapidly at brood-oven temperature, but 40° C. may prevent development.

As to both gross and microscopic appearances, the organisms studied fall into three groups:

First, the blastomyces form. The blastomyces described by Hektoen, that by Hessler, and one presented to-night are of this type. Growth is noted, after twenty-four hours, as small, elevated, moist, glistening, white points, which rapidly increase in size and soon coalesce to form a smooth membrane of pasty consistence. Threads soon penetrate the substratum evenly or in tufts (this property is rather inconstant and may disappear during prolonged cultural life). No aërial hyphæ form and the surface remains relatively smooth and glistening. Maltose and glucose solutions are fermented, alcohol and carbon-dioxid being formed. A similar organism described by Curtis produces acetic acid in the process of fermentation; however, no one of the three mentioned has this property. Saccharose and lactose solutions are not fermented. In bouillon a bottom growth occurs which may be uniformly disseminated by shaking. The example of this group which I have studied particularly forms indol slowly in Theobald Smith's sugar-free bouillon. Similar organisms described by others do not possess this property. They are all obligate aërobes. Microscopic examination of

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cultures shows the following forms: 1, branching hyphæ, made up of elongated segments, and possessing lateral, sessile or pedunculated conidia; 2, hyphæ, composed of chains of spherical or oval cells, which separate to form free conidia; 3, separated oval or spherical cells which proliferate by a building process. The budding cell predominates, and prolonged artificial life may result in the entire disappearance of mycelial forms.

Second, the oïdium form; represented by one organism in the present series. It develops on ordinary media in twenty-four hours and forms small grayish colonies which coalesce. The resulting membranous growth is at first finely granular, but eventually becomes deeply folded or disposed in small coils, and intimately and firmly incorporated with the medium. Glucose and maltose solutions are fermented, CO_2, alcohol, and acetic acid being formed. A membranous top growth, which falls in large flakes to the bottom, forms on liquid media. It does not produce indol, and, like the preceding organism, will not grow in the absence of oxygen. There are no aërial hyphæ, but short spikes may project above the surface. Microscopic study shows that it grows largely in the form of branching, segmented hyphæ, the segments gradually becoming spherical or oval, and separating successively from the chain. The loosened cells occasionally proliferate by budding, but more commonly sprout new threads. The formation of lateral conidia occurred at first in small degree, but has now ceased entirely. So the striking morphological feature is the formation of segmented hyphæ, which resemble oïdium in their life history.

Third, the hyphomyces form. The present series includes five organisms of this type. Growth is visible in for three to five days after inoculation of media (maltose preparations preferred), as a central point from which fine branching hyphæ radiate. An aërial growth may be noted in from ten days to two weeks, and in-

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creases rapidly. At the same time threads penetrate the substratum, the reverse surface of which gradually assumes a rich golden-brown color. A coherent, fluffy tuft forms in bouillon; no indol or acid is produced, and saccharine solutions are not fermented. Obligate aërobes. The aërial growth is found to consist of densely packed, branching, segmented hyphæ, bearing large numbers of lateral, pedunculated conidia, which may multiply *in situ* by budding, thus forming small clusters of conidia. A terminal body, resembling a spore-containing sac, is seen occasionally. The submerged mycelium is larger, but likewise segmented and branching, and produces a few conidia and unicellular offshoots. Conidia may multiply by budding, or they may sprout threads. The threads may break up into chains of conidia as noted under the second type. The structure of the individual cell is similar in all the organisms, but not always identical. Uniformly there are present a clear, refractive, doubly-contoured capsule and a central protoplasmic substance. The latter may be perfectly clear, but more commonly is differentiated into granules, and a nucleus-like structure, and, in some cases, into numerous refractive bodies which resemble spores. The adventitious capsule, which is often seen in sections of infected tissue, seems not to exist in cultures. What appears to be a clear, structureless space separating the protoplasm from the capsule, is sometimes recognized in living preparations, but is more conspicuous in dehydrated and stained specimens. Its nature is not clear. It is this form of organism which is associated with the eosinophilous type of the disease.

Diseased human tissue has been implanted in animals (particularly guinea-pigs) whenever possible; an inflammatory nodule usually develops in from two days to a week; in from one to two weeks the center may break down into thick creamy, or cheesy, pus, or the nodule may be absorbed without suppuration. If the pus is

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evacuated under aseptic conditions, pure cultures of the fungus may be obtained; if spontaneous evacuation occurs, mixed cultures are quite sure to result. No animal thus inoculated has ever contracted discoverable tuberculosis.

The results of the inoculation of pure cultures depend on the particular organism used, upon the animal inoculated, and the mode of inoculation. A sufficient number of animal inoculations has not been made to determine satisfactorily the pathogenicity of the various organisms for particular animals.

The blastomycetoid organism of this series, when injected subcutaneously into mice, invariably kills them in from 24 to 48 hours; similar inoculations into guinea-pigs and rabbits produce toxemia and local abscesses, which discharge and heal spontaneously; while in dogs there has been no perceptible disturbance. Intra-peritoneal inoculations into guinea-pigs produced no effect. Intravenous injections of rabbits and dogs produce septicemia which may be most profound, but from which all animals have thus far recovered. The fungus may be reclaimed in a pure state, from the blood and organs of mice which have died from inoculations, and from the subcutaneous abscesses which form in other animals. The guinea-pig brought for your inspection to-night illustrates the result of subcutaneous inoculation.

The oïdium-like organism of this series, so far, has been non-pathogenic to mice, rabbits and dogs, but caused subcutaneous abscesses in guinea-pigs.

Of the five hyphomycetoid organisms only one has received satisfactory pathogenetic study. A dog which received intravenously a bouillon suspension of a pure culture of the organism grew moribund after a lingering illness and was chloroformed. The lungs, exhibited to-night, were almost completely occupied by large, succulent, ill-defined nodules, in which were found vast numbers of a capsulated, spherical, budding and sporing

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(?) organism resembling those seen in the human tissue. An organism identical with the one inoculated was cultivated in a pure state from the nodules. Although no hyphæ were found in the lung tissue, when the latter was inocuated into a bouillon drop preparation, the spherical cells were seen to sprout threads which gradually acquired all the characteristics of those seen in culture tubes.

It will be seen that the organisms isolated form an ascending scale as to complexity. The simplest multiplies largely by germination of spherical or oval cells, but is able under suitable conditions to form branching, segmented threads which produce lateral conidia, or break up, oïdium-like, into concatenate conidia. The intermediate type grows by preference in the last named form, but its cells may also multiply by budding, and its threads are certainly capable of yielding lateral conidia. This form morphologically corresponds to oïdium, taking O. albicaus as the type. Certain cells, seen frequently, seem to indicate that endogenous spores may form, but further evidence is desired. The mold variety presents the highest organization. Both aërial and submerged hyphæ yield abundant conidia, and the former possibly bears ascospores also. As in the other varieties, however, spherical cells may proliferate by budding, and threads may be divided into chains of spherical or oval cells which are abjuncted successively. It seems quite certain that the mold type may produce endospores both in cultures and tissues; but, as before, further evidence is necessary for conviction.

Since the differences between the three types remain quit constant, it follows that they should be separated specifically. On the other hand, since these differences are for the most part differences in degree only, and not radical, and since the differing organisms appear as the cause of a clinical and histological entity, it seems proper to place them under a common genus. Hence,

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in accordance with the morphological and biological indications, it seems proper to consider these organisms members of the genus oïdium. Further study is desirable to determine satisfactorily specific nomenclature.

Busse's case illustrates that a fatal pyemia may be caused by an organism of the yeast, or blastomycetoid, type. It is of great interest in this connection to note the discovery by Ophüls and Moffitt, less than a year ago, that the so-called protozoic disease of Posadas, Wernicke, Rixford and Gilchrist and others, is caused by a mold fungus. The histopathology of the lesions in the skin, as described by Rixford and Gilchrist, is identical with that of "blastomycetic" dermatitis. Likewise the visceral anatomical findings are virtually identical with those in Busse's case of *saccharomycosis hominis*. Moreover, the organism isolated from a case of the "protozoic disease" by Ophüls and Moffitt, appears to be identical with the mold fungus presented to-night as the cause of five cases of "blastomycosis" of the skin. These conditions, in my mind, justify the belief that the three diseases named are caused by organisms which, though not necessarily identical, probably are offshoots from a common generic stem. That is, the above-named diseases constitute a group which in regard to its unity is quite analogous to actinomycosis and trichophytosis.

It seems strange, no doubt, that from the upwards of thirty cases of "blastomycetic" dermatitis so far described none has terminated in a generalized infection. I have knowledge, however, that an occurrence of this sort is soon to be made public. Still the rarity of metastatic complications is striking—as it is in tuberculosis of the skin. Possibly in both cases the safeguard is the underlying and surrounding areolar tissue, which is capable of accommodating such large amounts of reactive, and protective, inflammatory deposits.

The negative relation of these conditions to tuberculosis is shown by the facts that no animal inoculated

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with diseased tissue has died of tuberculosis as a consequence, and that tubercle bacilli have never been demonstrated in stained preparations of the diseased human tissue.

That they are not examples of carcinoma caused by parasites is shown by the fact that when metastases occur, they consist purely of the parasite, malignant epithelial cells never entering the circulation; furthermore, the histopathology of the two affections is radically different.

CONCLUSIONS.

I. From a study of the clinical histories and histopathology of eleven cases of so-called blastomycetic dermatitis, the independence and specificity of the disease seem beyond question.

II. Seven organisms isolated from seven of the cases fall into three groups: (1) blastomycetoid or yeastlike; (2) oïdiumlike; (3) hyphomycetoid; which appear to be separated by specific differences; morphologically and biologically they are included in the genus oïdium.

III. There are two histologic forms of the disease: 1, the eosinophilous, and 2, the non-eosinophilous; the former is associated with the mold form of the organism.

IV. The so-called protozoic disease of Posadas, Wernicke, and others; Busse's and Curtis' saccharomycosis hominis, and Gilchrist's blastomycetic dermatitis constitute a group of diseases possessing a closely related group of causes, i. e., the various species of the genus oïdium suggested under (2).

V. In accordance with (2) and (3) it seems wise to apply the term *oidiomycosis* to the group of diseases, and *oidimycosis of the skin* to the disease as it occurs in the skin.

It is, of course, needless to add that much work is yet to be done relative to the pathogenetic value of these fungi and their relationships.

April 8, 1901.

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BLASTOMYCETIC DERMATITIS OF THE GLUTEAL REGION.

FREDERICK G. HARRIS.

The history of this case is somewhat incomplete on account of the patient's mental condition, but so far as obtainable it is as follows:

Family History.—The patient is a woman, aged 78 years. Both her father and husband died from unknown causes. Her mother died of phthisis. She has had nine children; one daughter has phthisis, one son is living and well, one child died in infancy, two children died of yellow fever, and four are dead of causes unknown to the patient.

Past History.—The patient was born in Germany; lived in New Orleans for forty years, during which time she had yellow fever. She never had any other illnesses, denies venereal infection, and there are no stigmata present. She has lived in Chicago for the past ten years.

Present History.—Patient's present trouble commenced nearly four years ago, when she noticed a pimple on her left hip, which became a roughened area of intense itching, and later, on account of scratching, became apparently denuded of epithelium. The growth gradually increased in size and the itching persisted, but of much less intensity.

She was admitted to the Cook County Hospital as a case of syphilitic ulcer. A piece of the growth was excised and on microscopical examination a diagnosis of epithelioma was made and the patient transferred to the surgical service of Dr. Charles Davison, who has kindly permitted me to report the case.

The growth is on the upper posterior part of the left gluteal region; it is oval in outline, measuring 11 cm.

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long by about 6 cm. wide. The entire growth is movable on the underlying tissues. The border is quite hard, elevated about 8 mm., and in places the growth can be felt extending out into the surrounding skin. From the inner side of the border papillomatous growths overhang the floor; they are of various sizes, the largest measuring 2 cm. long. Most of these villous-like projections bear secondary and tertiary growths of a smaller size, the whole being covered with epithelium, giving them a bluish-white color similar to venereal warts. At no point on the border is there an area of ulceration indicating an extension of the process (Fig. 1).

The floor is covered with small fungoid epithelial growths similar to those projecting inward from the border. These papillæ vary in size from a small elevation to 0.5 cm. in height. Here and there among these elevations are darker red areas of ulceration, the whole floor being more or less covered with a hemorrhagic exudate. Extending in a diagonal direction nearly across the growth is a band of uninvolved skin about 2 cm. wide.

There are no secondary growths near, or, in fact, on any part of the body; but on the bridge of the nose is a hard, non-ulcerated, sessile tumor about the size of a hazelnut. It is freely movable on the bone, but the skin is closely attached to it. On the surface are seen several dilated blood vessels. This little tumor is painless. It has been there for the past twenty years, and the patient thinks it is due to the irritation of a pair of brass spectacles. It bears no resemblance whatever to the growth on the hip, and microscopical examination shows it to be an endothelioma.

The patient complains only of the itching, which is much less intense than when the growth started, but which at times interferes with walking; there has been no actual pain at any time. The neighboring lymph glands are but slightly enlarged.

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Pieces of the hip lesion were fixed in 4 per cent. aqueous formalin, dehydrated in alcohol, cleared in benzole and cedarwood oil, embedded in paraffin, and stained by various methods. The best results were obtained with eosin and polychrome methylene blue, but hematoxylin, followed by Van Gieson's stain, gave good results, as did also Weigert's elastic tissue stain. Sections stained for tubercle bacilli were negative, as were those stained by Gram's method.

Figure 1.

Microscopical Appearance.—Some distance outside of the growth the skin is normal, but on approaching the affected area the interpapillary processes of the rete mucosum are seen to extend deeper into the corium, and instead of being regular in form they often have knob-like projections from their sides, as if they were budding, and at their lower extremity they often bifurcate to enclose a mass of corium. This irregularity increases

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the nearer we approach the growth. At the edge of the growth we see the papillomatous outgrowths extending over the floor. They are seen to be formed by an extension of the corium, covered on both surfaces with epithelium, which extends into the interior in irregular projections.

In this core, so to speak, are irregular isolated masses of epithelium, many of which are hollow and contain corium infiltrated with round and plasma cells and leucocytes. Occasionally in these islands of epithelium we find the miliary abscesses which are so characteristic of this disease.

The floor of the growth shows villous projections similar to those described as growing inward from the border. From the surface of the floor there is a marked hyperplasia of the rete mucosum, which dips down into the corium in coral-like projections, branching in different directions or subdividing to enclose masses of the corium. Sometimes the cells in the center of these epithelial down-growths have become cornified and taken on a concentric arrangement simulating the pearls of epithelioma.

In other places are seen miliary abscesses, composed mostly of collections of polynuclear leucocytes, desquamated epithelial cells, more or less granular material, an occasional giant cell, and the specific organism. These abscesses are surrounded by flattened epithelial cells, the prickles of the outer layers being well preserved. The abscesses are most numerous deep in the corium, where the organisms and giant cells are also more common. The giant cells are of the tuberculous type; they are found more abundantly in the areas of round-cell infiltration which are present here and there, and especially where a miliary abscess has ruptured; once in a while a giant cell is seen containing the blastomycetic organism (Fig. 2).

The organism is the typical double-contoured circular

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or oval body having a mass of deeply staining, granular protoplasm, which is usually eccentrically placed, often containing one or more vacuoles. The organisms vary much in size and are found in groups of two or more, usually in the different stages of budding. They are not so numerous in this case as in some of those previously reported. They show a tendency to occur in the periphery of the abscesses or free in the corium where an abscess has ruptured, and are often surrounded by a

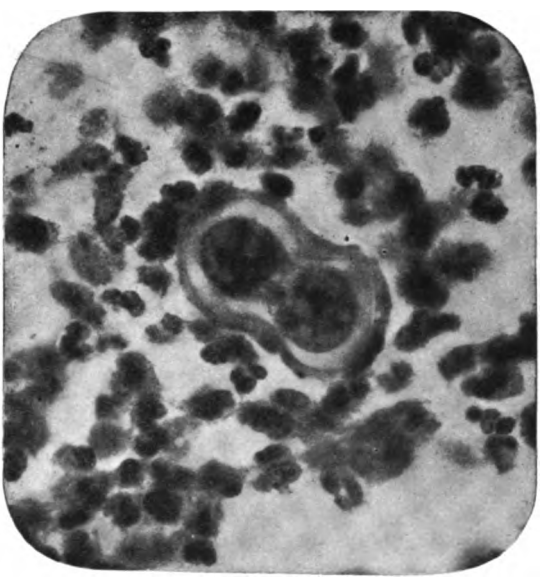

Fig. 2.—Budding form of blastomycetic organism. (Bausch and Lomb, 1/12.)

granular material which takes the eosin stain. I have been unable to find any organisms free in the rete or in the necrotic material covering the ulcerated areas.

The corium is well preserved and very vascular; the entire tissue is more or less edematous and shows a marked infiltration with leucocytes, which, while most numerous in the miliary abscesses, are also seen in great numbers between the cells of the epithelium, seemingly

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working their way toward the surface. There are vast numbers of polynuclear eosinophiles and plasma cells in the corium; mast cells are also not uncommon.

The appendages of the skin, hair follicles and glands have entirely disappeared.

Unfortunately there were no cultures made from this case.

The treatment consisted of complete excision of the affected area and the sliding of cutaneous flaps to cover the defect. With the exception of some sloughing of the flaps and the development of a pleurisy with effusion, the patient has made a satisfactory recovery, and there is no evidence of recurrence.

February 11, 1901.

A CONTRIBUTION TO THE HISTOGENESIS OF MELANOSARCOMA OF THE SKIN.

ALFRED SCHALEK.

The histogenesis of melanosarcoma of the skin has been in the last few years the subject of lively controversy. The opposing theories are entertained, advanced respectively, by Unna and Ribbert. It was the earlier opinion of pathologists that a melanosarcoma may originate, as does every other sarcoma, from any place in the connective tissue, and is distinguished only by the pigment, which is formed by the tumor cells; in other words, a melanosarcoma was classified as a species of sarcoma. The first investigator to contest this opinion was v. Recklinghausen, who asserted that pigmented nevi and the melanosarcomata arising from them, origi-

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nate only from a particular variety of connective tissue cells, namely, from the endothelia of lymph vessels and clefts.

An entirely new theory was advanced by Unna in 1893, who claimed that melanosarcoma of the skin does not originate from connective tissue at all, but from epithelia, which at some time have been cut off from their original site and have become surrounded completely by connective tissue. Hence Unna insists that these tumors must be classified as melanocarcinomata and not as melanosarcomata. To quote from him: "Alveolar carcinomata of the skin are rare; a part of these are the carcinomata originating from nevi; that is, the nevi carcinomata." The tendency of these tumor cells to detach themselves from the surface epithelia and to form alveolar nests is the result of a metamorphosis, or, as Unna calls it, "metaplasia," of the epithelial cells. Another proof of their epithelial origin, according to Unna, is the total absence of any intercellular substance. He admits that an error in the diagnosis is possible, because of the fact that the distribution of the pigment occurs independently of the proliferation of the epithelial cells, so that the connective tissue may be studded with pigment before there is any appearance of epithelial proliferation; this may easily lead to the deceptive conclusion that connective tissue elements form the tumor. Unna claims further to have seen in pigmented nevi of new-born children the gradual separation of the nevi cells from the surface epithelium and their metaplastic changes. He concludes: "Epithelial cells separate from the epidermis during embryonic development or in early infancy, and these cells, included in connective tissue, may thus remain latent until at some later time under the influence of some stimulus they begin to grow and form malignant tumors. These tumors can only be regarded as melanotic alveolar carcinomata."

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Unna's opinion was later adopted by others, among them Krohmayer[2] and Delbanco.[3] The latter made his observations on one pigmented and one unpigmented nevus of a child, and describes the invasion of connective tissue between the epithelial pegs, whereby these pegs become fringed and thinned out, until they finally lose their connection with the surface and become entirely surrounded by conective tissue. These separated epithelia lose their prickles, so that they resemble the surrounding connective tissue cells, but still retain their vesicular, deeply staining nucleus and the polygonal shape of the cell body. These cells represent the typical tumor cells. Simultaneously with this process the connective tissue cells proliferate. "In old nevi," as Delbanco says, "this proliferation of connective tissue and the separation of the epithelia have come to a standstill and the *status nascendi* can no longer be seen." In contradistinction to Unna, Delbanco observed lymph vessels inside of the nests of the nevi cells, with endothelial cells surrounding these nests, a picture which he explains as due to the growth of proliferating nevi cells into the lymph crevices. This probably caused v. Recklinghausen to look upon the endothelial cells as a matrix, from which the tumor originates. Delbanco believes, like Unna, that the pigment is not a determining factor in the genesis of the melanosarcomata.

An entirely different view is presented by Ribbert,[4] in whose opinion melanosarcoma is undoubtedly of connective tissue origin; but, according to him, not every connective tissue cell can give rise to melanosarcoma, but only a specific cell *a priori* adapted for it. While other authors have previously held that the pigment and its distribution in the melanosarcoma was entirely independent of the growth of the tumor, Ribbert asserts that a melanotic tumor can only originate from a special connective tissue cell, which produces pigment, namely, the "chromatophores." Basing his arguments on the

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identity of the melanosarcomata of the skin and of the eye, Ribbert makes the following statement: "Since the pigment cells of the choroidea are characteristic in their shape and their production of pigment, and can not be identified with any other connective tissue element, it is certain that the tumor cells also, which originate from them, must represent special cells that can not be mistaken for the elements of any other sarcoma, even if they appear similar in their shape and type." Ribbert best demonstrated these chromatophores in teased fresh tissues of a melanosarcoma, where they appear as polymorphous branched elements, which contain pigment, variable in amount and distribution. Between these other cells are found, of a round or oval shape, with a coarser and denser pigmentation, which are identical with the cells above described, but are in a state of contraction. In stained specimens, where the branched cells may lie in a parallel arrangement, they may closely resemble a spindle-celled sarcoma. In older tumors the transitional stages are lost and the cells forming the new growth present themselves in simpler forms. "As melanosarcomata of the eye arise from the chromatophores of the choroidea, so the melanosarcomata of the skin arise from pigmented nevi, which represent proliferations of pigment cells." The difference in appearance between the chromatophores and the nevi cells, which latter are round and often free of pigment, is explained by Ribbert as due to their being in a different stage of evolution.

Gilchrist,[5] in a recent publication on melanosarcomata and pigmented nevi, confirms Unna's views and says: "Since the epithelioid cells which make up the structure of the mole are of epidermal origin, any malignant growth springing from these cells should be regarded as of a carcinomatous and not sarcomatous nature."

Johnston,[6] who made the histologic examination in Foster's unique case of congenital multiple nevus pig-

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mentosus, also endorses Unna's conception as to the epithelial nature of congenital pigmented nevi.

To this discussion of the histogenesis of the melanosarcomata of the skin, full of interest as it is, to both pathologist and the dermatologist, I desire to contribute the results of some observations, made upon five cases, as follows: Two of pigmented nevi, two of melanosarcomata of the skin, and one of a melanosarcoma of the nasal mucous membrane. The last case, though not directly pertaining to the subject under discussion, presents some features of interest, which bear upon it. The specimens described were partly sectioned in series and were stained by various methods, such as hematoxylin-eosin, Van Gieson's stain, Weigert's stain for elastic fibers, and others.

Pigmented Nevus I.—If one examines this nevus under low power one sees that the epidermis has become flattened and thinned out, the papillary layer has entirely disappeared and interpapillary pegs are consequently not present. The epidermis consists of four or five layers of epithelial cells only. The epidermal have a round, vesicular nucleus, not very rich in chromatin, and a moderately large, more or less cuboidal, cell body. The basal layer contains a finely granular pigment. The sub-epidermoid layer consists of wavy connective tissue fibers, with a few nuclei only. Within it we find a tissue, composed of cells, which are of the character of embryonal connective tissue cells. The nuclei are vesicular, variously shaped, round, oval or fusiform. These cells form roundish, more or less irregular nests, in which large thin-walled blood vessels can occasionally be seen; any fibrillar stroma is not present. In some places the cells in the cell nests contain a large amount of coarsely granular brown pigment; some cells show one or more processes, and have the character of chromatophores. Free pigment is also found between the cells. Weigert's stain for elastic fibers shows that the finest

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terminal elastic filaments enter between the epithelial cells of the lowest layer. The pigment in these cells is more coarsely granular than in the layers above. Some of these cells deviate from the cuboidal or round to the branched and stellate form. In this manner the impression is conveyed that the stellate and branched cells are descendants of the pigmented cells in the epidermis.

Pigmented Nevus II.—This nevus shows in general the same structure as the first one, excepting that the cell nests found in the corium are distinctly surrounded by fibrous tissue, so that apparently real elveolar nests are formed, the same as are found in a true carcinoma. We find here likewise pictures which strongly suggest that the pigmented epithelial cells of the lowest epidermal layer proliferate between the elastic fibers into the connective tissue become entirely surrounded by the latter, and assume, after a number of transitional stages, the character of stellate chromatophores.

Melanosarcoma of the Skin I.—The epidermal epithelium stretches over the neoplasm in a thin, slightly wavy layer, covering a tissue consisting of cells which look very much like epithelial cells, having large vesicular nuclei, not very rich in chromatin, and fairly large cell bodies of a round or oval, or more or less irregularly polygonal shape. This tumor tissue is fairly rich in strongly pigmented cells, which are fusiform or stellate in outline. The cell masses show a network of lymph clefts, around which the pigmented cells show a marked tendency to arrange themselves. This picture has evidently caused von Recklinghausen to maintain that melanosarcomata originate from lymphatic endothelium. In some places there can be recognized the same transition of the epidermis to the characteristic pigmented cells of the tumor proper, as has been described above for nevi.

Melanosarcoma of the Skin II.—In this specimen

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the interpapillary pegs of the epidermis are rather larger in size; the prickles between the epithelial cells are distinctly visible in the lower layers. Pigment is found both in the epithelium as well as in the lower cells. The latter have no alveolar arrangement, but infiltrate the upper part of the corium in a diffuse manner. Fusiform connective tissue is not found between the tumor cells, but is markedly increased in the lower part of the corium. This tumor is richly vascularized, and shows well the arrangement of the tumor cells around the vessels. This grouping of cell masses around the vessels gives the tumor the appearance of glandular structure. The endothelia of the vessels are sharply defined from the surrounding cells proper. Some of these latter, which are isolated from their connection with the main mass, show particularly well the resemblance to epithelial cells by their large polyhedral body and vesicular nucleus; other cells are polynuclear giant cells of moderate size. Pigment is present in both the epithelial and connective tissue parts; in the former filling up the epithelial cells, but leaving their shape intact and their nuclei visible. The pigmented connective tissue cells present the type of chromatophores.

We desire to include in our consideration the histology of a melanosarcoma, which does not properly belong to the melanosarcomata of the skin; it is one of the nasal mucous membrane, and is here included in our discussion because its structure appears to furnish some very valuable points. Unfortunately, this specimen comes from a tumor recurring after the first removal, and consequently does not enable us to demonstrate beyond doubt where the tumor originally started from. But in examining it carefully it presents every evidence of having started from the surface epithelium. In the superficial part of the tumor we find typical alveolar nests, surrounded by fusiform connective tissue cells. The tumor cells have a large vesicular nucleus, very rich in

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fine granular chromatin, with quite a large polygonal cell body. They show a good deal of polymorphism; occasionally cells are seen which contain two, three or more nuclei. A large percentage of the tumor cells contain a dark brown pigment; the pigment granules are of medium size. In the deeper parts of the tumor, pigment cells are also found in the interalveolar connective tissue septa, where they assume the character of chromatophores. They become stellate and the pigment granules are much coarser than those found in the cells of the cell nests.

In other parts the chromatophores are found to be situated on the outside of vessel walls; it appears that they have proliferated and formed in places quite extensive tumor masses around the blood vessels. In this manner the impression is created that we are dealing with an endothelioma, and this impression is still strengthened by the fact that such tumor masses around vessels infiltrate the neighborhood in a diffuse manner, the cells themselves becoming fusiform or more or less of the character of chromatophores. It appears that the histogenesis of this decidedly heterogeneous tumor may be best explained as follows: The new growth started from pigment proliferated into the connective tissue, became entirely surrounded by it, lost their character of epithelia, assuming that of chromatophores; some of these wandered toward the vessel walls. Such an assumption appears to be reasonable in view of the observations of Jacques Loeb, who found in fish embryos that the chromatophores show a special affinity for blood vessels and creep to their walls. This observation, made several years ago, has been confirmed by others. It is, therefore, not at all astonishing, but quite as we might anticipate, to find a similar occurrence in a pathological process. In the nasal tumor above described the cells proliferating around the vessels give those parts in which this process is going on very markedly the appearance

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of an epithelioma. If, however, we compare this nasal tumor with the pigmented nevi and the melanosarcomata of the skin, we must strongly incline to the conception above, namely, that this melanotic tumor is of epithelial origin, showing transitional stages in an unusually well-marked manner.

If, now, in conclusion, we attempt to formulate an opinion as to the histogenesis of melanosarcoma of the skin, we must concede that the final decision is by no means easy, but fraught with many difficulties. But it appears that the standpoint taken by Unna and followers is probably correct. Melanosarcomata of the skin do arise from pigmented epithelial cells of the epidermis; these cells proliferate into the connective tissue and become entirely detached from the epidermis; still further proliferating, after having been cut off, these cells lose their epithelial character and assume that of ordinary connective tissue elements and that of those particular pigmental cells known as chromatophores. This view, that epithelial cells may undergo such a metaplasia under pathological conditions, is not at all improbable, since L. Loeb[6] has experimentally demonstrated that such a change may take place, when epithelia are implanted into connective tissue. L. Loeb[7] has also stated in another paper that chromatophores of a typical character originate from epithelial cells. Concerning the pigment we have found that it is finely granular and not very dense in the epithelial cells from which the melanotic tumor arises. The pigment becomes more coarsely granular, the more pigmented cells assume the character of connective tissue cells, more particularly that of chromatophores.

In conclusion, I wish to express my thanks to Dr. Maximilian Herzog, to whom I am indebted for the material and for kind suggestions.

March 12, 1900.

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REPORT OF AN ANATOMICAL TUBERCLE.

MARTIN H. FISCHER.

In July, 1899, while sewing up the body of a tuberculous subject after postmortem, I pricked the skin over the second interphalangeal joint of the middle finger of the right hand. No blood was drawn. About a month later a small indurated papule developed. Two months later it had grown to the size of a pea. At times it would become fissured and a drop or two of serum would exudate. A histological examination of the serum showed polymorphonuclear leucocytes but no bacteria. Five months after the accident the nodule had grown to the size of a coffee-bean, and was surrounded by a considerably reddened areola. The movement of the joint was somewhat interfered with and there was slight sensitiveness. March 3, 1900, the nodule was removed by Dr. Arthur D. Bevan.

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Histological examination shows the following: The epithelium is much thickened; beneath this, in the corium, is found a circumscribed area of infiltration surrounded by a thick wall of connective tissue. Over part of the infiltrated area the granular layer of the epithelium is lost; in the remaining portions it is present but it has lost its sharp definition. A few polymorphonuclear leucocytes are found in the epithelium. The infiltrated area is sharply defined by a thick connective tissue wall. The infiltration is mainly of the small mononuclear variety, but some few polymorphonuclear leucocytes are found. Numerous whole and fragmented giant cells are scattered through the inflamed area. There is slight central necrosis of the central portion of the diseased focus. At the periphery are seen numerous fibroblasts. Vessels are found in the inflammatory area but no blood corpuscles are discoverable. Outside the large inflammatory focus are small areas of infiltration.

The attempt to find the tubercle bacillus in the tissue resulted negatively.

The growth recurred at the site of the scar and at the end of April, 1900, was represented by an erythematous area the size of a nickel. In the central part of this was a pea-sized papule. To one side, in the line of the scar, there developed two pinpoint-sized caseous areas. On June 1, the two caseated areas were cauterized with carbolic acid. The erythematous area continued to exist, but no other areas of caseation developed. The inflammatory process has evidently healed as nothing but a slightly reddened scar remains. (September 12, 1900.)

The case is an interesting one in so far as we have to deal with the reproduction, histologically at least, of tuberculosis after a positive inoculation from a positively tuberculous subject. This satisfies Koch's laws.

May 14, 1900.

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CARCINOMA OF SEBACEOUS GLANDS OF A RAT.

LEO LOEB.

The tumor had grown in a few months to the size of almost half the head of a rat. It was ulcerating. It grew again to its original size inside of a few weeks after partial removal.

Microscopically one sees enormously large sebaceous glands, branching out in different directions. At some places the skin covers the glands. The new-formed tissue takes after some time the appearance of sebaceous glands. At other places one sees deep in the connective tissue more or less changed, isolated sebaceous glands. They may form alveoli of spindle-shaped cells. That demonstrates (*a*) direct outgrowth of glands as the first change in carcinoma; (*b*) morphologic anaplasia of tumor cells is not a primary factor underlying carcinomatous change.

November 12, 1900.

H. T. RICKETTS read a paper entitled "A Histological Study of an Endothelioma of the Skin."

June 11, 1900.

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MISCELLANEOUS.

ON THE PRESENCE OF NEW ELASTIC FIBERS IN TUMORS.

ALICE HAMILTON.

The question of the participation of elastic fibers in the hyperplasia of connective tissue has recently aroused a good deal of attention, especially since the discovery of differential stains has made possible the recognition of very delicate elastic fibers. Sclerotic blood vessels seem to have been first and most extensively studied with a view to ascertaining not only the fate of the elastic fibers in the media, but also the nature of the newly formed fibers in the intima. Langhans[1] was the first to declare that this new tissue consisted largely of elastic fibers, and later Baumgarten[2] and Heubner[3] confirmed this view. More recently Dmitrijeff[4] and Jores,[5] working with better staining methods, have described in detail the processes occurring in arterio-sclerosis. Though they find minor differences in the syphilitic and non-syphilitic forms, the process in the main is found to be the same in all, namely, a granular disintegration and final absorption of the elastic fibers of the media followed by an extensive proliferation of elastic fibers in the intima. The thickened intima, in fact, consists almost wholly of delicate elastic fibers.

Both Jores and Dmitrijeff consider that the growth of these fibers in the intima is compensatory, to make up for the loss of elasticity in the media, but they differ in opinion as to the rapidity of their formation. Dmitrijeff finds them always in the older parts of the tissue

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and thinks they are the result of a slow chronic process, while Jores finds them appearing in the very early stages of endarteritis proliferans. This opinion is confirmed by recent researches of Czyhlarz and Helbing.[6] Jores believes that endarteritis proliferans should not be classed as a chronic inflammatory process, since it differs from such in any other tissue in this one important characteristic—the production of elastic fibers instead of white fibrous connective tissue. The hyperplastic connective tissue which results from chronic inflammation in other tissues, does not, according to his view, ever consist of elastic fibers. This assertion is disproved by the recent investigations of Melnikow-Raswedenkow.[7] He seems to be the first who has systematically studied, by Weigert's staining method, the normal distribution of elastic fibers and the question as to their increase in different pathological processes. His investigations include the liver, spleen, lymphatic glands, heart, adrenal, and testicle. His conclusions are as follows: In hyperplastic connective tissue there is in almost all cases a proliferation of elastic fibers. This proliferation is always compensatory in character either to make up for a loss of elasticity in the organ, or to increase its normal elasticity. Thus in cirrhosis of the liver, the induration and loss of expansibilitv caused bv the new connective tissue is not so great as it would be were the new tissue not composed largely of elastic fibers. In cicatricial contractions, especially in the myocardium, the new tissue contains many elastic fibers to diminish the evil effects of the contraction. In chronic passive congestion when the organ must force on a large volume of venous blood, we find the new tissue very rich in elastic fibers. On the other hand, when there is no need for elasticity the new tissue consists simply of the white fibrous variety, as in the thickened capsule of chronic perisplenitis and in the sclerotic patches in serous membranes. In almost all cases he finds these

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fibers derived from the adventitia of the blood vessels; the fibers grow slowly and are very resistant to degenerative changes.

The formation of elastic tissue being thus always compensatory, always for a definite purpose, Melnikow-Raswedenkow thinks there is no reason why they should share in the formation of new growths which are entirely harmful in character; and as a matter of fact, he finds that they do not play any part in such growths. He does not enter into the subject in detail, but states that he has formed this conclusion from the study of many cases of benign and malignant neoplasms; and mentions adenofibroma, fibromyoma, sarcoma, carcinoma simplex and scirrhus, cystoma glandulare. He thinks that the frequent occurrence of degenerative changes in the center of new growths is due to this lack of elastic fibers in their stroma and the consequent imperfect circulation.

I have been unable to find anything definite on this last subject in the writings of other authors. Apparently the question as to whether elastic fibers might not play a part in the formation of connective tissue tumors has never been thoroughly investigated; neither is there any information to be gained as to their presence in the stroma of epithelial growths and of those sarcomata which contain a stroma. It would seem at first sight entirely possible that, inasmuch as all forms of connective tissue are found as elements of tumors, this one variety should also be found, either as a minor part of the growth or forming its chief constituent. Also, considering that the stroma of tumors is formed from the stroma of the organ in which the new growth occurs, it would seem quite possible that when this organ is rich in elastic fibers the newly formed stroma should also contain them, as it contains new blood vessels.

In investigating this question as to the participation of elastic fibers in the formation of neoplasms I chose the Weigert stain,[8] which gives very excellent results, ir-

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respective of the hardening fluid used. It can be used without counter-stain, the blue-black fibers standing out against a light blue or almost colorless background; or, if it is desirable to stain the cells, the counter-stain advised by Weigert, lithium-carmine, may be employed. A good contrast is obtained with hematoxylin and eosin, but a much more striking one by rapid treatment with Van Gieson's stain and hematoxylin. In such sections the cells are stained yellow, nuclei brownish, the white fibrous tissue pink and the elastic fibers blue-black.

As most investigators are agreed that the formation of elastic fibers in hyperplastic connective tissue is a slow process and that the new fibers come from the pre-existing ones, I looked for the best results in benign connective tissue growths occurring in tissues normally rich in such fibers, and therefore selected first for examination fibromata of the subcutaneous tissue. The result in most cases was disappointing. Elastic fibers were present in narrow strands between bundles of white fibers, but in such small numbers that it was impossible to be sure that they were not the pre-existing fibers of the subcutaneous tissue which had been pushed apart by the new growth. In only one case were the fibers more numerous, irregularly scattered in thick twisted bundles. This same appearance was found in a myofibroma of the uterus. Better results were gained from adeno-fibroma and pericanalicular fibroma of the mammary gland where the proliferation of elastic fibers was often quite extensive. In the normal mammary gland elastic fibers of moderate thickness are found forming bands around the excretory ducts, while a few very delicate ones may be seen in the stroma between the lobules. In the above named neoplasms these bands around the ducts are often increased in thickness and fibers can be seen running out into the surrounding tissue, while thick bundles of fibers are found in the interacinous stroma as well as in the stroma between the lobules. The elastic tissue of the

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adventitia of the blood vessels is increased and sometimes the fibers pass out into the surrounding tissue. In none of these cases, however, did the elastic fibers form a conspicuous element of the tissue, and in some they were very scanty in number. No tumor of this class was found which consisted of elastic fibers exclusively.

Turning then to the question of their presence in the stroma of tumors I chose as the most promising the scirrhous carcinomata. The tumors examined were from the pancreas, mammary gland and liver. The distribution of elastic fibers in the normal pancreas is similar to that in the mammary gland, namely, in slender bands around the excretory ducts, a few delicate fibers in the interlobular tissue, and of course in the walls of the blood vessels. The liver is much more abundantly supplied with these fibers, which are present in such large numbers in the interlobular connective tissue that they seem to leave little room for any other sort of tissue. Almost all of the scirrhous carcinomata from these organs which were examined for this purpose were found to contain large numbers of elastic fibers far more than had been found in any of the fibromata examined. The fibers in some cases seemed to come from the pre-existing ones around the ducts or vessels, but were far more abundant than in normal tissue and passed from these regions to the surrounding stroma. This was especially true of the two cases of scirrhus of the liver, originating in the bile duct epithelium. Not only the stroma of the new growth but the hyperplastic connective tissue throughout the organ consisted largely of elastic fibers which radiated from the adventitia of the blood vessels and bile ducts. In scirrhus of the pancreas the elastic fibers were not so numerous and were found in thick masses scattered irregularly in the stroma of white fibrous tissue. Two cases of scirrhus of the liver and one of the pancreas showed a peculiar arrangement of these fibers. They formed a series of quite well-marked

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FIG. 1.

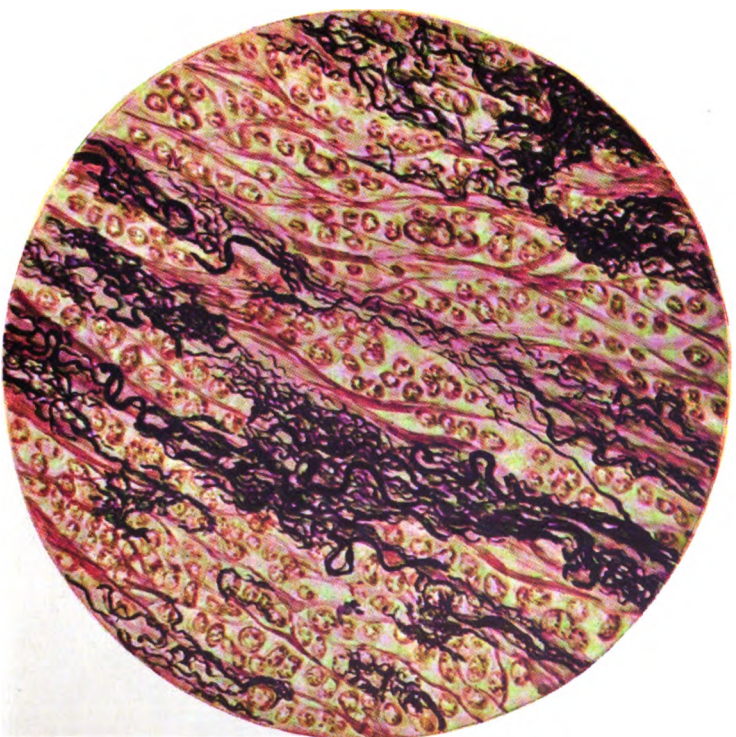

FIG. 2.

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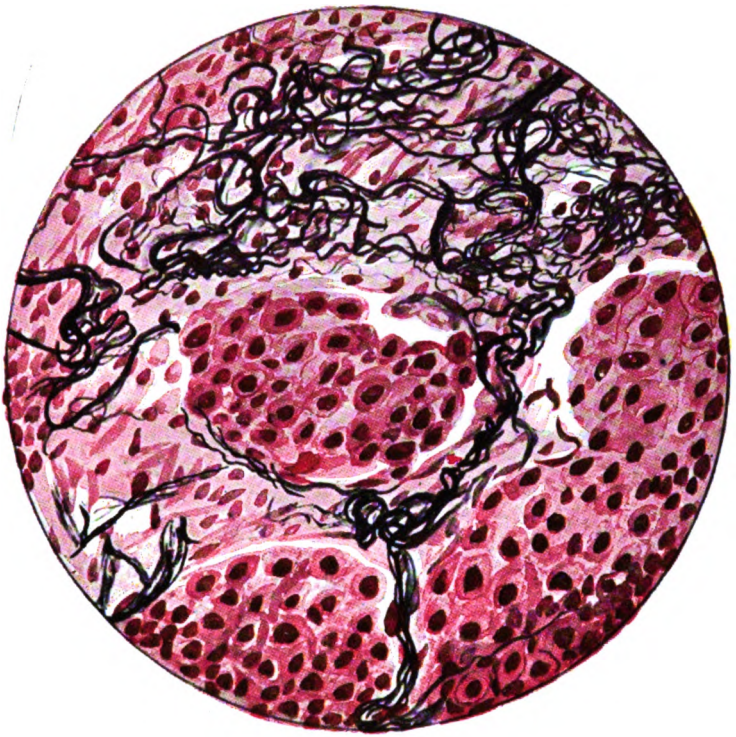

FIG. 3.

FIG. 4.

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concentric rings around a center which was made up of carcinomatous cells in nests lying in a stroma quite free from elastic fibers. This appearance might be explained by the more rapid growth of this portion of the tumor, which had pushed aside the elastic fibers of the more fully developed stroma. Such an arrangement does not show at all in sections stained by the usual methods.

In scirrhus of the mammary gland the elastic fibers were found around the excretory ducts, around the nests of cancer cells and in the interlobular connective tissue. In some these fibers were delicate, wavy, arranged in regular bands; in others, thick, short, twisted, arranged in heavy masses. Always the appearance was characteristic of elastic fibers, the variable thickness of the fibers, the wavy outline and curled ends. Usually they occurred in scattered groups, but occasionally they were woven in with the stroma quite evenly. In almost every case they formed a conspicuous element in the new growth.

Contrary to expectation, it was in the soft, malignant tumors of epithelial origin, where the connective tissue stroma was delicate and there was every evidence of rapid development, that the richest growth of elastic fibers was found. In adenocarcinoma of the uterus, stomach and mammary gland, the stroma in many instances consisted largely of elastic fibers, and very seldom were they altogether wanting. In several cases these fibers were found only in the thicker trabeculæ of the stroma and in two instances the deeper part only of the tumor contained them, the fibers ceasing gradually as the margin of the growth was approached.

The only forms of sarcoma which promise success in such an examination are fibrosarcoma and alveolar sarcoma, and good results were obtained in examples of both these groups. A melanotic alveolar sarcoma showed thick, twisted bands of elastic fibers in the stroma; a fibrosarcoma showed delicate wavy fibers passing between the cells. In neither of these two was there any

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apparent connection between these fibers and those in the adventitia of the blood vessels, but in a fibro-sarcoma of the brain this connection could be plainly seen. This tumor, which I have described before this Society, evidently originated in the outer walls of the blood vessels and possessed a stroma entirely made up of elastic fibers, which ran in bands, radiating from the vessels, or were collected in rosettes. In this case all of the fibers were elastic—in the other two the background for these fibers was made up of slender bands of white fibrous tissue.

It may be objected that the elastic fibers found in these tumors are simply those which were already present in the tissue in which the growth occurs. In answer to this several arguments may be advanced to prove that there is in the cases described a formation of new fibers which is sometimes very extensive. In the first place they are found in tumor masses where there is no question that we have to do with a newly formed stroma, not an infiltration of the original tissues. In the second place they are found in numbers far greater than those normally present in the organ affected. Thirdly, they are found in scattered masses not in connection with vessels or ducts, although normally the organ in question contains elastic fibers only around the excretory ducts and blood vessels. Thus in a case of scirrhus of the pancreas the elastic fibers are abnormal in quantity and arrangement. Indeed, the number found in the tumor often bears no relation to that normally present in the tissue in which the growth occurs. Several specimens of carcinoma of the uterus contained a stroma very rich in such fibers, while two examples of carcinoma of the lung and several of carcinoma in subcutaneous tissue contained none at all. In scirrhus of the liver different parts of the same tumor show different numbers of these fibers and their arrangement is very often, as in the pancreatic and mammary tumors, entirely different from that in the normal organs.

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The term "proliferation," as applied to elastic tissue, is, of course, rather loosely employed. Strictly speaking, "formation" or "deposition" would be more accurate, though an exact term can not be found until the nature of the process is better understood. The dispute between histologists as to the cellular or intercellular origin of these fibers is still maintained, and the same lack of agreement is found among those who have studied their formation under pathological conditions. Langhans and Dmitrijeff from their study of arterio-sclerosis conclude that the fibers originate in the intercellular matrix, while Heubener and Jores, working upon the same sort of tissue, decide in favor of their cellular origin. It is impossible for me to speak decidedly on this point from my observations of new growths, but it is certainly true in my experience that the tumors containing the largest numbers of elastic fibers are those which possessed a stroma comparatively rich in connective tissue cells, which would seem to indicate that the cells play an important part in the formation of these fibers.

February 12, 1900.

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Fig. 1.—Scirrhous carcinoma of the pancreas, showing elastic fibers arranged in rings around a central area. Weigert's stain—counterstained with lithium carmine. Leitz, Obj. 3; Oc. 3.

Fig. 2.—Alveolar carcinoma of the mammary gland. Weigert's stain—counterstained by Van Gieson's method. Leitz, Obj. 6; Oc. 3.

Fig. 3.—Alveolar carcinoma of the uterus. Weigert's stain—counterstained with lithium carmine. Leitz, Obj. 6; Oc. 3.

Fig. 4.—Fibro-sarcoma. Weigert's stain—counterstained by Van Gieson's method. Leitz, Obj. 3; Oc. 3.

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REPORT OF THREE CASES OF PERIOSTEAL SARCOMA.

PAUL F. MORF.

CASE 1.—Ernest A., American, aged 13 years, schoolboy. Admitted to the Presbyterian Hospital, Chicago, April 10, 1899. His family history is negative. There is no record of any tumor. He has always been healthy, with the exception of the usual diseases of childhood. His present trouble began about one and one-half years before admission to the hospital. While playing football he received a kick on the inner side of the right leg, midway between the knee and the ankle. This injury was followed by the appearance of an area of discoloration from 3 to 4 cm. in diameter. No swelling was noticed until about one week later, when a small prominence about 3 to 4 cm. in diameter developed at the seat of the injury. This swelling was only slightly tender; it did not become any smaller, but after existing about one month, began to increase in size. The growth was at first very slow, but about four months before he came to the hospital (by which time the tumor was about as large as a hen's egg) it began to enlarge rapidly. The patient had little or no pain until about one month before admission, when he began to suffer some pain at the inner side of the knee-joint of the affected side. Some time previously he received continuous treatment (presumably antisyphilitic) which caused no change whatever in the neoplasm.

This patient was operated on by Dr. N. Senn. Amputation at the knee-joint (Gritti-Stokes). I am indebted to Dr. Senn for the privilege of presenting the case.

The tumor (Fig. 1) consists of a large, somewhat

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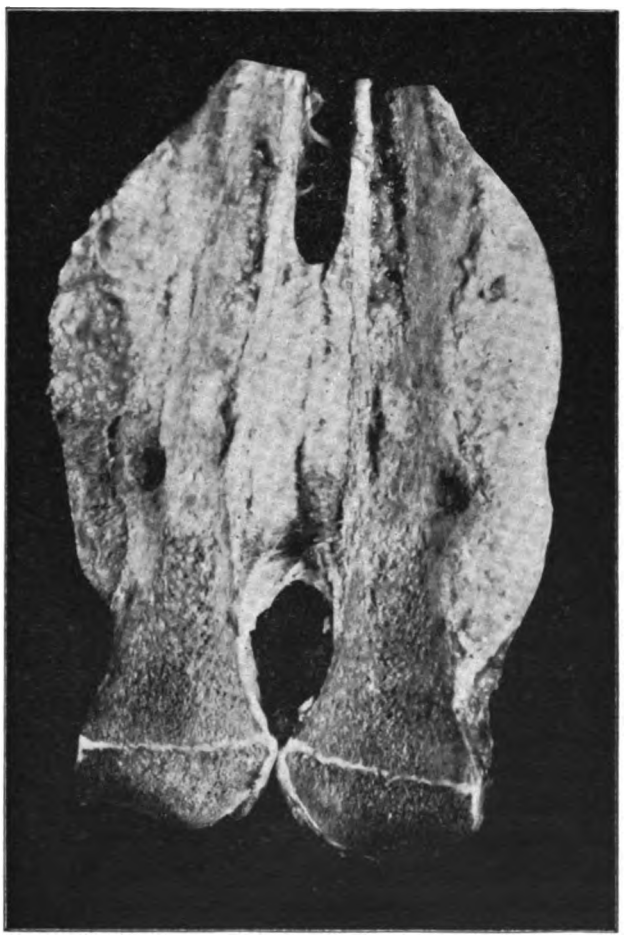
spindle-shaped mass surrounding the upper part of the tibia more or less completely. On cross-section it has a mottled grayish and white appearance, the matrix



Case 1.

being formed by the grayish tissue, with numerous small white islands of apparently cartilaginous substance embedded in it. The tumor causes grating when cut, and

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on passing the finger over the cut surface numerous fine sharp points may be felt. On closer inspection these rough points are seen to be small semi-transparent granules of calcium salts, varying in size from that of a pin point to that of a pinhead. These are embedded in the white glistening firm islands, these latter being from 1 to 5 mm. in diameter and of an irregular outline. Microscopically the matrix is found to be made up of small spindle cells. The white areas are identical in structure with hyaline cartilage, except that the cartilage cells are larger and more numerous than usually seen in normal hyaline cartilage. The areas of hyaline cartilage end with abrupt margins and are sharply defined; they do not shade gradually into sarcomatous tissue.

The cortex of the tibia has been invaded by the sarcoma cells. Near the medulla of the bone are Haversian canals filled with the usual structures, while preceding toward the more peripheral layers of the cortex numerous canals, some of which are greatly increased in size, are more or less completely filled by spindle cells.

The neoplasms, therefore, belong to the group of chondro-sarcomas, and from its location and origin may be designated a peripheral or periosteal sarcoma.

CASE 2.—Ed. W., aged 19; occupation, farmer. There is no history of tumor or malignant growth in the family. The personal history has no bearing on the present trouble. This began gradually about August, 1898. The patient at first noticed that the right knee-joint felt tired after exertion. This feeling of fatigue soon gave place to a dull, aching pain in the same location, which was especially noticeable in the morning. The pain gradually increased in severity, radiating along the hamstring muscles. About Jan. 1, 1899, he noticed a slight swelling about the patella. This swelling gradually increased in size and was more noticeable at the inner than at the outer side of the knee. In spite of

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the pain and swelling the patient was able to walk until April, 1899. About one month before this time the leg began to be drawn up into a position of flexion, the deformity becoming more and more pronounced up to the time of operation in August, 1899. The limb was amputated about the middle of the thigh by Dr. Christian Fenger, whose kindness in permitting me to report the case I wish to acknowledge. The tumor consists of a large club-shaped mass occupying the lower fourth and lower articular extremity of the femur (Fig. 2). Macroscopically the neoplasm differs but little from the specimen described above. Histologically it also resembles this tumor very closely, being a small spindle-celled sarcoma containing cartilaginous foci, some of which are partly calcified.

CASE 3.—K. G., female; aged 21; single. Family history is negative. Personal history.—The patient has always been quite well, with the exception that she has had the usual diseases of childhood. Present trouble began in November, 1898, more or less insidiously, with pain in the region of the left knee. In February of the following year the knee-joint on this side began to become somewhat swollen. Since then up to the time of admission to the hospital the pain and swelling have progressively increased, and the leg has been drawn up and flexed to an angle of about 40 degrees. Since the time the present trouble began the patient has been losing in weight and strength and has become markedly anemic. She has an evening temperature ranging from 99 to 100.2° F. In spite of the cachexia the appetite has remained fairly good. The treatment in this case consisted in amputation of the left thigh at the hip-joint by Wyeth's method. The operation was performed by Dr. A. E. Halstead, to whom I wish to express my thanks for the case. The lower chain of inguinal glands on the side corresponding to the tumor were found moderately enlarged and were, therefore, also removed.

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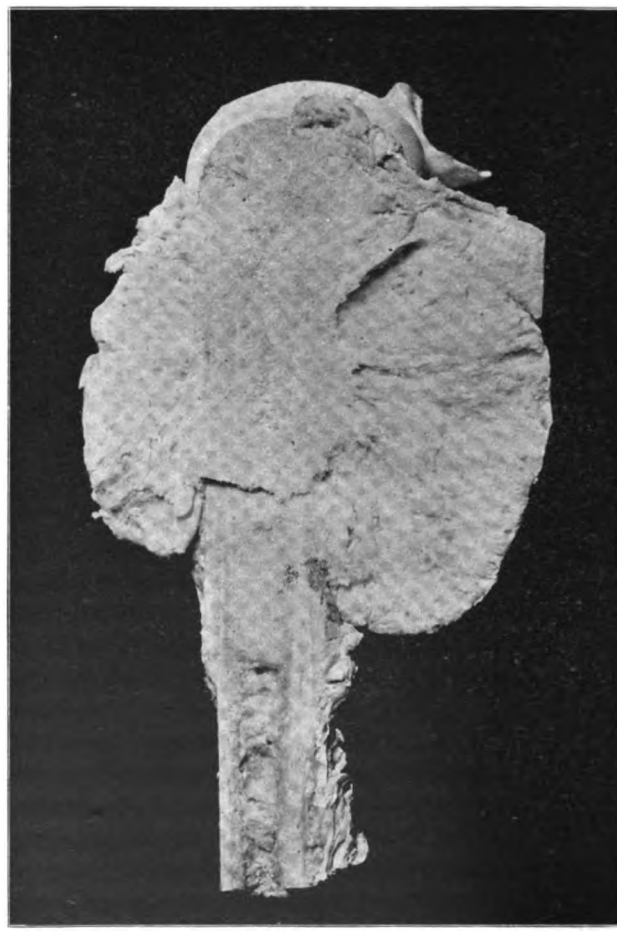
Healing of both wounds followed per primam. Up to January 10 of this year there had been no recurrence. Patient then reported herself well, having gained about 60 pounds in weight.



Case 2.

The microscopical examination of the inguinal glands failed to show any metastases. The tumor proved to be

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a small spindle-celled sarcoma with a few small areas of cartilaginous tissue scattered throughout its substance and here and there a small focus of myxomatous degeneration.

These three tumors are examples of periosteal or peripheral sarcomas, since they evidently had their origin in the periosteum. According to Bland Sutton ("Tumors, Innocent and Malignant," p. 79) this variety of neoplasm occurs earlier in life than the central sarcoma of bone and is frequently associated with antecedent injury. These tumors also show some tendency to invade the medulla of the bone when situated on or about its shaft, the embryonal cells reaching the medulla by way of the Haversian canals. (This was noticed in Case 1 v. s.) They have a predilection like central sarcomata for the joint ends of the bone. (Cases 2 and 3.) They are liable to calcification and ossification, to a greater degree than the central sarcomas. This tendency, as Sutton points out, is not surprising when we remember that "bone-making is the essential function of the periosteum. The crystal-like spicules so frequently found in these tumors doubtless represent ossifications of the fibrous trabeculæ, which normally connect the periosteum with the compact tissue of the bone. As the periosteum is raised from the bone by the growing tumor the trabeculæ elongate and afterwards ossify into spicules." The slight tendency to the formation of metastases may be explained by the fact that for a long time these tumors are covered by the periosteum, which acts as a rigid barrier to regional and general dissemination of the embryonal cells.

Histologically these tumors to some extent resemble the hyperplasia which occurs when bone and periosteum have been injured (e. g., fracture). The question has even been raised by competent pathologists whether these neoplasms should be regarded as tumors in the more restricted sense of the term rather than be considered as

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a hyperplasia of periosteal cells, resulting from some chronic irritation. The frequent history of antecedent injury gives plausibility to this view. However, in the light of our present knowledge or, rather, lack of knowledge, as to the exact relationship which exists between normal hyperplasia of these structures (viz., bone and periosteum) and the cause of true malignant bone tumors, it seems proper, at least for the present, to class them with the true sarcomas, since they resemble these malignant growths in their tendency to invade the bone (Case 1) and the occasional occurrence of metastases.

January 14, 1901.

MULTIPLE PRIMARY MALIGNANT TUMORS: REPORT OF A PRIMARY SARCO-CARCINOMA IN THE THYROID OF A DOG, WITH MIXED SARCOMATOUS AND CARCINOMATOUS METASTASES.

H. GIDEON WELLS.

Combinations of carcinoma and sarcoma in the same individual are naturally of two classes:

1. Each form of tumor occurring as a separate growth, either distinct from each other or near together, but having no structural relation.

2. Carcino-sarcoma or sarco-carcinoma—that is, a neoplasm presenting the two distinct types of malignant growth, as a combination which forms a single primary tumor.

Concerning the first class, we know nothing about tumors that should prevent a patient with a sarcoma

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from having a carcinoma elsewhere in the body, or conversely. Such a combination is to be looked upon simply as an accidental occurrence, and under the laws of chance likely to occur occasionally. If not found more frequently than is to be explained by chance, these multiple diverse malignant tumors can not be considered as of any particular significance. Such a combination has been occasionally observed.

In 1896, in connection with the occurrence of multiple primary malignant tumors, M. Walter collected six cases in which each of the two tumors was of a different type. Briefly they are as follows:

CASE 1.—Becker reported the case of a woman, aged 52, with a rodent ulcer of the left side of the nose, removed by operation. A melano-sarcoma was present on the right cheek, arising from a pigmented mole. On the right auricle and on the right upper eyelid typical epitheliomas existed as separate tumors. No metastases developed.

CASE 2.—Niedergall had a case in which existed a papillary carcinoma in the left upper angle of the uterine cavity, a mucous polypus in the upper part of the cervical canal, a submucous myoma on the posterior wall; and the site of a tumor which had been expelled spontaneously showed this tumor to have been a "fibro-sarcoma reticulo-cellulare polyposum." This specimen was obtained by hysterectomy, and no secondary growths developed.

CASE 3.—Thierfelder, in a 70-year-old cowherd, found a spindle-celled sarcoma of the stomach, and a squamous-celled carcinoma of the esophagus. Metastases were not mentioned.

CASE 4.[1]—A 78-year-old woman had a typical duct-carcinoma of the head of the pancreas, while in the liver were found multiple "primary angiosarcomas." No metastases were observed.

CASE 5.—Kretz found endotheliomas of the dura mater, and a carcinoma of the esophagus in a man aged 46. In the right femur were metastases of both varieties of growth, apparently not mixed.

CASE 6.—Scheven, in an idiotic, epileptic male, aged 44, found multiple psammomas or psammo-sarcomas in the left striate body, and in the outer part of the right ventricle. Both kidneys were greatly enlarged, especially the left, by a mixed tumor containing fatty tissue, smooth muscle cells, and sarco-

1. Augusta Hospital in Köln, November, 1894; reporter not named.

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matous portions. A walnut-sized clyindrical-celled carcinoma was present in the stomach. No metastases were reported.

To this collection may be added the following:

CASE 7.—Griffon and Dartignies give the case of a man, aged 50, who had been operated on three years before for a tumor of the kidney, diagnosed as "cancer" and probably a carcinoma, who died of a squamous-celled carcinoma of the esophagus. The renal tumor had not recurred. Five months before death a fibro-sarcoma appeared on the back of the hand.

CASE 8.—Phillipson reports a case, a man, with sarcomatosis of the skin, who had carcinomatosis of the internal viscera, the largest mass, which was perhaps primary, being in the gall-bladder.

CASE 9.—Scheel, at the autopsy on a 70-year-old woman, found a scirrhous carcinoma of the mamma, and a spindle-celled sarcoma of the right ovary.

CASE 10.—Rabl-Rückhardt reports the case of a woman who spontaneously expelled a sarcomatous mass from the uterus, while in the uterus itself a carcinoma infiltrated the wall extensively. The authenticity of these findings is under dispute—v. Kahlden accepts them, but Emanuel does not.

CASE 11.—Emanuel describes the case of a woman, aged 47, who was hysterectomized for malignant growth. A polypoid mass, which microscopically was a small round-celled sarcoma, projected from the posterior uterine wall. The mucous membrane lining the remainder of the uterus was thickened and full of papillary projections, due to a "carcinomatous degeneration," of the type of malignant adenoma. The two types of growth were distinct and individual. No recurrence occurred after operation, and no metastases were reported.

v. Franque reports three cases occurring among sixteen cases of sarcoma of the uterus, as follows:

CASE 12.—From a patient, aged 48, a specimen was obtained by hysterectomy; this showed a primary sarcoma of the interstitial submucous connective tissue of the body of the uterus, round-celled with some giant cells. In the cervix was a beginning gland carcinoma. A few metastatic particles of sarcoma tissue were present on the surface of the ovary—from implantation, apparently—and a few similar particles were present in the lumen of the Fallopian tube. The patient died some time after the operation, presumably of recurrence, but the body was not examined.

CASE 13.—Woman, aged 50. Hysterectomy, no recurrence or evidence of metastases. A papillary adeno-carcinoma was present in the lower part of the uterus, extending into the cervix.

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In the cervix was a round-celled sarcoma. The two growths were quite distinct, each being presumably primary.

CASE 14.—Sarcoma of the wall of the uterus, with metastases in the vagina and broad ligament; the specimen was removed by hysterectomy. About 1 cm. below the internal os and 3 above the external os was a very small area in which proliferation of the epithelium had formed a carcinomatous structure. This carcinoma was very young, the growth being but about ½ mm. in thickness.

C. F. Beadles quotes the two following cases:

CASE 15.—Blackburn reports the case of a man, aged 80, who died with senile dementia, in whom were found: 1, endothelial sarcoma of the dura mater; 2, carcinoma of the stomach, a typical columnar "adenoid carcinoma"; 3, round-celled sarcoma of the right testicle. These three were independent, primary growths. There were secondary growths in the lymphatic glands about the cœliac axis and down the spermatic cord, and also in the left kidney. This last-named growth was examined and found to be like the testicular growth, a round-celled sarcoma.

CASE 16.—Mann and Stranahan report the case of an insane man, aged 72, with advanced epithelioma of the penis, who had a large endothelioma of the dura mater, situated over and greatly destroying the left temporo-sphenoidal lobe of the brain.

Beadles also mentions the case of a woman with carcinoma of the breast, who, for thirty-three years, had had a recurrent subcutaneous tumor in the right iliac region, which he considers a "'recurrent fibroid tumor,' a variety of spindle-cell sarcoma." As no histological study was made, and the tumor evidently not being truly malignant, although recurring, it is not to be classed with the multiple primary malignant tumors.

CASE 17.—Simon records the case of a patient with generalized melanotic sarcoma, originating in the right eye. At autopsy, in addition to a remarkably extensive deposit of secondary growths, a white nodule was found in the liver which resembled a non-pigmented sarcoma nodule, or at least was supposed to be such. Microscopically this white nodule was found to be a typical cylindrical carcinoma, from its structure presumably arising from the gastro-intestinal tract, which unfortunately had not been examined at the autopsy.

These being all the reasonably authentic cases that can be collected, it is apparent that the simultaneous appearance of sarcoma and carcinoma is not of frequent occurrence. The presence of one variety of malignant tumor does not seem to predispose the individual to

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develop the other type. Judging from its rarity the multiplicity of the growths is simply fortuitous, as suggested previously, and has no significance to the pathologist as to their biology, unless it be in a negative way.

Tumors composed of a mixture of the epithelial and mesoblastic type are of much more interest, and the cases already reported are as follows:

CASE 1.—Kaufmann, in his article on malignant tumors of the thyroid, describes this case: A man, aged 67, died in 1871. At the autopsy the right lobe of the thyroid was found to contain a nodular, irregular tumor, twice as large as a fist, reaching from the hyoid bone to the jugular vein. The isthmus was immediately connected with it, and joined it to the left lobe, which was a little enlarged, and presented the appearances of common follicular struma. On microscopical examination a fibrous nodule, with the distinct structure of an ordinary fibroma, was found in the center. Near by this fibrous portion was a definitely sarcomatous tissue. Spindle cells, showing occasionally oblong and oval forms, were in uniform arrangement, with distinct intercellular substance. The vessels almost always lacked a wall of their own, presenting themselves as round spaces in the tumor tissue, but where the wall was visible it was demonstrable that it was in direct contact with the tumor tissue. This sarcomatous structure formed the whole of the tracheal portion of the tumor. Opposite the isthmus the extension of the sarcomatous into the thyroid tissue could be observed. The periphery showed a quite different structure, presenting the typical structure of a carcinoma, containing numerous cancer nests composed of multiform cells, cylindrical epithelium being distinctly demonstrable, and in size and general features resembling that of the thyroid vesicles. The stroma surrounded these nests and showed an alveolar structure when isolated. Carcinoma and sarcoma united directly, and in places it seemed as if the interstices between the carcinoma nests were filled with sarcoma tissue, which spread out among the nests but did not compress them, and was always distinctly limited and differentiated from them. This transition zone of carcinoma and sarcoma was relatively small, for the interstices filled with sarcoma quickly became smaller, and at last entirely lost the cellular elements. From its microscopical structure it was a fibro-sarco-carcinoma. In the kidney cortex a hazel-nut-sized mass was found, but it was not examined microscopically. The condition of the lymph glands is not mentioned.

CASE 2.—Kummer reports that a tumor, resembling clinically a strumitis, was removed from a female, aged 55. It pen-

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etrated the capsule of the thyroid, and a thrombus was found filling the left inferior thyroid vein. Bacteriological examination of the growth gave negative results. Death resulted soon afterwards with symptoms of a catarrhal pneumonia. Pulmonary metastases were suspected, but no autopsy was permitted. Microscopically the tumor was found to be of an adeno-carcinomatous structure, with areas of fusiform cells, in places replacing the glandular structure, and showing the characteristics of spindle-cell sarcoma. Kummer considers that the adenomatous portion is of parathyroid origin, because of the cylindrical character of the cells. The thrombus mentioned consisted of about four-fifths fibrin, and the remainder of adeno-carcinomatous structure, without presence of sarcoma tissue, from which he argues that the carcinoma was the more malignant of the two growths.

Thse two cases are the only ones found in the literature, in which a primary tumor seemed to consist of both sarcoma and carcinoma, and neither of these is complete. In the second—Kummer's case—there is no doubt that there was a malignant epithelial growth, as shown by the extension of carcinoma tissue into the vein. Kummer is also probably quite right in assuming that the spindle-celled growth was a sarcoma. However, the failure to obtain a complete autopsy leaves open the possibility, which is, of course, far from a probability, that this mesoblastic growth was simply a metastasis from some primary tumor elsewhere. Kaufmann's case is open to the objection that the malignant nature of the growth was determined by microscopic evidence only; the nodule in the kidney was not studied, so it can not be said that it was from the thyroid tumor. Again, it might be said that these growths represent simply the coincidence of two primary tumors in the same organ, which had met by extension, much as the double tumors of the uterus might have done if they had grown for a long enough time. The intimate relation of the two growths, particularly in Kummer's case, is against this view. While admitting that each of these cases was in all probability exactly what the reporter considered it, the conclusive evidence was lacking. Such evidence

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would be the positive exclusion of other primary tumors, and the demonstration of secondary growths representing each type, or, better still, growths containing both sarcoma and carcinoma in the same metastatic nodule. A case fulfilling these requirements has fallen into my hands, and is herewith reported.

The specimens were removed from the body of a Skye terrier bitch, about 12 years old. The animal had been ill for several months with cough and progressive emaciation, a veterinary surgeon who saw the case diagnosing it as pulmonary tuberculosis. Previous to this she had been perfectly well. The sufferings of the animal were so severe that it was killed by administration of prussic acid.

At autopsy the following conditions were found:

Thyroid greatly enlarged, especially the right lobe which was as large as a goose egg. The right lobe was honeycombed on the cut surface, from which a grumous fluid escaped; fleshy nodules were present beneath the capsule, or in it. The left lobe was somewhat smaller, honeycombed to a less extent than the right, and contained many fleshy masses like those in the capsule of the right.

Lymph glands about the thyroid were much enlarged, one mass being 3 cm. long and 1.5 cm. thick, studded with nodules which when cut yielded a milky fluid. The peribronchial glands were moderately enlarged, firm, and fleshy.

Lungs.—Both were filled with nodules, from those the size of a millet seed to some 2 cm. in diameter, somewhat lenticular, and semi-fluctuating; when they were cut a purulent-looking fluid escaped from the tissue, but did not leave a cavity. They were not located in any particular part of the lungs, both of which were equally involved throughout. The large bronchi and trachea were not affected.

Heart.—A white nodule about half as large as a split pea was found beneath the endocardium of the left ventricle.

A few similar small nodules were found under the capsule of each kidney, and a few the size of a pinhead were found under the serous membrane of the small intestines. The other organs showed no changes, and no other growths could be found elsewhere.

A piece of the tumor tissue was implanted subcutaneously in a guinea-pig, and cultures were made aërobically and anaërobically. These experiments all resulted negatively.

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Histological examination showed a most interesting condition, especially in the thyroid, where the growth was primary, as shown by the advanced condition of the process, the structure of the tumor, and the evident metastatic nature of all the other growths. Briefly, the thyroid presents the picture of an alveolar carcinoma—a true colloid carcinoma—plus a sarcomatous growth, of the angio-sarcoma or perithelioma type, which is in intimate relation to the more abundant carcinomatous tissue. The metastases were of various types. The cervical glands show only the carcinomatous structure. The nodules found in the kidneys, heart, and intestines consist solely of the sarcomatous growth, and seem exactly like the metastatic nodules found in a simple case of angio-sarcoma. In the lungs most of the nodules are carcinomatous, but some contain both types of growth, just as it occurred in the primary tumor. No nodules of the pure sarcoma were found in the lungs, but only a small proportion of the vast number of metastases here could well be examined. Small areas of cells similar to those in the sarcoma were found infiltrating the peribronchial glands.

More minutely the carcinomatous growth, alike in primary growths and metastases, is of the following structure: For the greater part it consists of small round cells, which at the periphery infiltrate the surviving tissues, and elsewhere form large masses in which are found small alveoli-like formations. The smaller of these alveoli do not contain colloid, the larger contain colloid that does not differ structurally from that of the gland tissue itself, except perhaps that it is a little less dense. The round cells are small, and perfectly spherical, the nucleus is usually deeply stained and forms the greater part of the cell, but when isolated a narrow rim of protoplasm is found surrounding it. Where the alveolar formation is at all evident, a distinct cuboidal epithelial type of cell is produced, exactly like the normal thyroid epithelium, but where the cells are abundant the mass seems to consist of a dense accumulation of nuclei with a slight homogeneous and fusing intercellular substance. The alveolar arrangement is seen even in the most dense growths, at least as a slight tendency for these round cells to collect into groups with a central lumen, and in this way the round cells can be seen to be of the same nature as the alveolar cells, *i. e.*, epithelium. Serial sections show these structures to be true closed alveoli, not tubules or duct formations. The stroma is very scanty, and where found is distinct from the round cells, which tend to be arranged as a slender row lying along it. Blood vessels are very numerous, always with a distinct layer of connective tissue outside the endothelium, and separating it from the tumor cells. Leucocytes are absent, and karyokinetic figures are seldom seen.

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The sarcoma growth is very different in appearance, and where both types occur together the contrast is striking; there can be no doubt that they are entirely different forms of neoplasm. In these cases, as a rule, connective tissue lies between parts of the line of junction of the sarcoma and carcinoma, but in many places the former infiltrates the latter, and the spindle cells may sometimes be said to form the stroma for new-formed alveoli. Islands of sarcoma tissue are found in the carcinomatous portions, generally radiating out from vessels; and, conversely, isolated masses of carcinoma tissue are present in the sarcoma. The cells of the sarcoma are poor in protoplasm, and a distinct cell wall is not visible, but only oblong nuclei are outlined. Where the protoplasm of individual cells can be found, it is seen to trail out at each end from the nucleus, thus forming a "large spindle-cell." Generally, these cells are parallel, and they tend to be perpendicular to a blood vessel, radiating from its thin wall of endothelium and connective tissue, thus giving the typical structure of a perithelioma or angio-sarcoma. The vessels are very numerous, and, as a rule, the smaller ones have their walls made up of tumor cells, generally with a distinct layer of endothelium. Karyokinetic figures are abundant. In the kidney, heart, and small intestines, the metastatic growths show no carcinomatous structure in any portion when studied in serial sections, but are solely of sarcomatous tissue.

Beyond these three cases no records of what may be called a primary growth of sarcoma and carcinoma can be found. Bennet has reported a tumor of the thyroid gland removed from a young woman because it caused pressure symptoms. Microscopically the tumor he describes is an adenoma with a center suspiciously like a sarcoma. Whether these structures were or were not malignant is not determined. Förster,[1] in discussing carcinoma of the thyroid, states that the ordinary carcinoma is occasionally observed in combination with sarcoma. The antiquity of this observation and the lack of detail prevents its inclusion here.

The very interesting fact is developed that all the three probable, as well as the two doubtful, cases occurred in the thyroid, and this is all the more strange because of the relative infrequency of malignant tumors

1 "Text-Book of Pathology," 1863.

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of this organ. To be sure many reports have been made of such mixed tumors arising in the uterus, but careful examination of all such reports shows them to be either two separate tumors or else mistakes in histological diagnosis. The mistake usually has been that of considering the hyperplasia of the large-celled submucosa of the uterus as sarcoma, although von Kahlden has pointed out this error in discussing the papers of Abel and Landau, on carcinoma of the cervical portion of the uterus with "sarcomatous degeneration" of the mucous membrane of the body of the uterus. Fränkel and Wiener also remark on a deceptive condition frequently present in the structure of old carcinomas. As the epithelial cells age, retrogressive changes occur in them, the protoplasm disappearing until only a small amount is left about the nucleus and the periphery of the cell, which then assumes a certain resemblance to reticular connective tissue. If, in addition, the nuclei lose some of their affinity for stains the resemblance to sarcoma becomes still greater. In this way certain old inoperable carcinomas, in which only such altered portions happen to be investigated, are readily mistaken for sarcoma. This would, of course, also be a possible source of wrong diagnosis of mixed sarcoma and carcinoma. Von Kahlden considers the case reported by Rosenstein to have been a sarcoma, while Kuhner's and Keller's cases are probably carcinoma. Under the heading of "sarco-carcinoma" have been variously described endothelioma, perithelioma, alveolar-sarcoma, sarcoma of the choroid, and other melanotic malignant tumors, by different writers, particularly in the literature of over a decade ago, when the tumors, of endothelial origin especiallv. were not understood.

Taking these cases together, it is seen that the only case completely and positively verified as a true mixed tumor of carcinoma and sarcoma is the one now reported in this paper, since it is the only one in which the metas-

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tases have been studied. As the histology of a tumor is rarely absolute evidence of its malignancy, the absence of metastases or the failure to study them always leaves some room for doubt. This has been the case in the so-called mixed tumors of the uterus, for either metastases have been wanting or when present have been of but a single type. In the case under discussion the fact that not only were metastases found containing only carcinoma cells or only sarcoma cells, but also secondary growths of mixed structure duplicating the primary growth, is of especial value. That the subject was a canine does not lessen the value of the observation, since dogs and other animals develop the same sorts of tumors as does man. On looking at the sections above described one would not for a moment question that they were from a human being, so far as the histological structure of the tumors is concerned. Dogs are very frequently affected with disease of the thyroid, and, where goiter is endemic, dogs suffer equally or more than man. Casper states that carcinoma is quite frequent in dogs. It occurs in unaltered as well as in strumous organs, and exists partly as soft cylindrical and partly as squamous-celled carcinoma. Especially characteristic, he says, is its breaking through into the lymphatics and veins, and the lungs often contain many embolic growths. None of the observations on malignant tumors in the lower animals obtainable mention a mixture such as has just been described (*vide* M'Fadyean, Casper and others).

Naturally the question arises, What is the significance of this great rarity of mixed malignant tumors in considering the general etiology of malignant neoplasms? From the ground of Cohnheim's theory we should be justified in expecting that mixed tumors would be frequent, perhaps the rule, since most of the "embryonal matrices" with which we are familiar, containing epithelial cells, also contain a connective tissue stroma, which proliferates with the epithelium when it develops

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into a tumor. Yet the stroma of adrenal tumors, arising from misplaced adrenal tissue in the kidney, does not assume a sarcomatous appearance. The nearest approach to this is seen in the renal tumors of mixed structure, the embryonal adeno-sarcomata of the kidney, which represent not only the epithelial and connective tissue structures, but also contain muscle fibers. These tumors, however, owe their malignancy entirely to the sarcomatous portions, the epithelium always being of an adenomatous type, never infiltrating the stroma, although the cells are of the appearance of the embryonal epithelium of the kidney. Renal embryonal adeno-sarcoma affords evidence that all of the structures of the fetal kidney may develop together and form a tumor, according to Cohnheim's views, but evidently it is a marked exception for both the stroma and the epithelium to become malignant at the same time, although the reason for this is not clear.

Considering neoplasms as the result of infection by organisms, whether protozoal or vegetable, we find the ideas as to the "specific cause" vary, in that some investigators consider that carcinoma and sarcoma are due to a single organism, which produces an epithelial tumor when growing in epithelium and a connective tissue tumor when growing in connective tissue, while others think that the cause of sarcoma is different from that of carcinoma, although perhaps closely related. If the same organism were capable of causing carcinoma and sarcoma we should expect that it would frequently set up malignant proliferation in both tissues at once, thus causing mixed tumors of carcinoma and sarcoma to be common, which is contrary to the fact. If, on the other hand, the organism that causes carcinoma is different from the one causing sarcoma it would probably be the rule that tumors would be of one class or the other alone, except in the rare event of a mixed infection with each of these hypothetical parasites, either together at the

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onset, or one infection implanted on the other, as is usually the case in mixed infection with known organisms. This idea agrees with the demonstrated infrequency of mixed malignant tumors, although the agreement is of no more significance than each observer wishes to give it.

The question of cellular specificity also arises, Is it possible that cells may develop either into epithelium or connective tissue, or into both, independent of which type the parent cells were? One of the strongest arguments in favor of the doctrine of cellular specificity is the unanimity with which epithelial cells produce carcinomas only, while connective tissue cells produce sarcomas and not carcinomas, and the absence of development of carcinomas from tissues containing no epithelium. If each cell did not produce its own kind, mixed malignant tumors should be common. I can only say that in the sarco-carcinoma studied, nothing was found that in any way suggested a transformation of epithelium into sarcoma cells, or conversely.

Why these primary mixed tumors are, so far as can be collected, always in the thyroid gland, is another interesting problem. In the first place, malignant tumors of the thyroid are not frequent, although there is no organ in the body (unless it be the adrenal, and even that is questionable) that is so prone to have "embryonal rests" scattered about in its vicinity, from the remnants of the thyro-glossal duct to the nests of thyroid tissue sometimes found within the hyoid bone, not to mention the islands of undeveloped tissue in and beneath the capsule. Most of the malignant tumors arising from the thyroid are carcinomatous, generally of a glandular type, often reproducing, quite closely, thyroid tissue, even in remote parts of the body, and this tumor tissue is sometimes capable of performing the function of the gland. Sarcoma is relatively rare; Morf in 1899 was able to collect but forty cases, although a few more have been

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reported since then. The occurrence of mixed tumors in the thyroid is therefore particularly hard to explain. There seems to be nothing peculiar about the stroma of the thyroid or the relation of the stroma to the epithelium, that gives any suggestion.

As conclusions derived from the study of mixed tumors, these statements may be made:

1. Carcinoma and sarcoma may occur simultaneously in the body of an individual as separate growths. This combination is no more frequent than is readily explained by assuming it to be a mere coincidence, and there is no evidence that the presence of carcinoma in any way predisposes the individual to development of sarcoma, or conversely.

2. Sarco-carcinoma, a tumor composed of malignant growth of both types, is even more rare. But three authentic cases can be found, and each of these originated in the thyroid. Metastases were studied in only one, and here not only were some of the secondary growths of mixed type, but pure sarcomatous and pure carcinomatous secondary growths were also found.

3. These facts may be of interest in considering the etiology and biology of malignant neoplasms, but they do not offer a direct explanation of any of the existing problems.

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March 12, 1900.

CASTRATION TUMORS IN SWINE.

H. DUNCAN.

There is a disease of swine occurring chiefly in the male, following castration, characterized by a peculiar and distinctive fibrous growth, which develops in the castration wound. It is a not uncommon affection among the swine herds in the Southwest, as Kansas,

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Missouri and Nebraska. As to the percentage of animals affected it is difficult to say, but it is possible that about 5 per cent. of the male animals are affected. Most of them never come to market. Those which do find their way to the stock yards are condemned by the government inspectors, who call the growths scirrhous tumors of the cord. A small fraction of those coming to the yards escape the eye of the inspector, as shown by the statistics furnished by Dr. Day, government inspector at the Viles Robbins packing-house, Chicago. Of 143,568 hogs inspected by Dr. Day during the months of July and August, 1898, 23 were condemned on account of suppurative swellings in the scrotum. These figures show that it is quite rare among the swine slaughtered in the great packing-houses.

The clinical history of the animals affected is about as follows: Within two or three weeks after castration a swelling appears, occupying the position of the testicle. Usually but one side is affected; occasionally two tumors make their appearance, merging later into one growth or remaining as separate tumors. The tumor, as a rule, grows rapidly, and in from three to five weeks after the inception of the growth one or more ulcers appear, usually in the cicatrix. Close inspection shows the ulcers to be the external openings of fistulous tracts, from which a thick, light yellow, pyoid material exudes in small quantities, sometimes in large amounts. Sometimes there is a serous fluid, constant but in small amount. The ulcers rarely heal. The growth frequently acquires enormous proportions as compared with the weight of the hog, and in such cases usually drags upon the ground. During the earlier stages of the disease the animal has a good appetite and thrives; a noticeable action of the animal thus affected is the constant switching of the tail. Later when, on account of the weight and position, the tumor becomes an encumbrance, the animal loses flesh and grows very slowly, but continues

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to have a good appetite. Still later in the disease, when it becomes a positive load to carry or drag the tumor about, the hog has a cachectic appearance. The animal usually dies a violent death, being killed by the owner, or run over by a wagon or trampled by cattle. Otherwise it usually dies within twelve to eighteen months from the appearance of the growth. The fact that in the later stages the animal is unable without considerable effort to obtain food and drink may hasten its death. The growths have never been observed to heal spontaneously. Much more rarely a similar growth is observed in the female, usually on the breast.

The growth appears to be invariably in connection with the spermatic cord and is in most cases single, but there may be two or more masses on the same side of the scrotum. It consists of a softened center enclosed by a capsule of varying thickness of firm, avascular, white, fibrous tissue. Externally there is no distinct capsule, the firmer fibrous tissue merging more or less gradually into loose fibro-myxomatous tissue. The growth, when large enough, invades the surrounding muscles. The skin covering the tumor is firmly adherent and always includes the scar from castration. The form of the swelling is generally round or oval; the larger may present various sized protuberances and irregularities. Not infrequently there are smaller secondary tumors or nodules in close relation to the primary growth, varying in size from a pea to as large as a hen's egg. These secondary nodules have a structure similar to that of the primary growth. Occasionally several small tumors are found scattered along the course of the spermatic cord. In all cases the interior of the growths contain one or more cavities. The size of these vary greatly and bear no definite relation to the size of the growth. A tumor weighing 5 kilos may contain an area of softening as large as a walnut, the rest of the tissue being firm and white, or there may

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be a huge cavity containing a l. or more of turbid, thick fluid, the fibrous wall being from 4 to 16 cm., more or less, in thickness. Even the smallest nodules no larger than a pea contain a central area of softening. The contents of the cavity may be a soft, spongy, yellowish material adherent to the walls, or there may be a thin or thick turbid yellowish fluid; between these extremes are all possible transitional appearances. The necrotic material has a penetrating, somewhat sweetish, rather sickening odor, which is very characteristic. The margins are, as a rule, abrupt, and generally the solid tissue shows a more or less brownish discoloration for 0.5 cm. or so away from the margins.

During the summer of 1898 there was an opportunity for removing a number of specimens from the live animal. The following spring a series of tumors were obtained through the kindness of Dr. Day. These tumors were examined macroscopically and microscopically, and cultures were made which were placed under the ordinary and anaërobic conditions. In all more than twenty specimens were examined. Swine and guinea-pigs have been inoculated with pure cultures of organisms isolated from the tumors, and one inoculation was made with a small piece of necrotic tissue from one of the growths. This work was done in the Pathologic Laboratory of Rush Medical College.

The histology of the growth is comparatively uniform. As a rule there are four distinct zones in a section cut perpendicularly to the surface, which correspond to the description of the gross specimens. A section stained with hematoxylin and eosin shows externally a zone consisting of branching and spindle-shaped cells which stain well. The protoplasmic processes of the cells frequently anastomose. The intercellular substance stains feebly, taking, as a rule, an admixture of the acid and basic stains. Portions of the field may show a faintly striated eosin-staining intercellular substance.

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Next is a wide zone corresponding to the dense white tissue, which shows many spindle, oval and roundish cells, the nuclei of which are granular and stain well. Karyokinetic figures are sometimes seen. With methylene blue orcein quite a few mastzellen are noted, but no typical plasma cells. Blood vessels are not numerous. Some are atypical, the walls being very thin. Others appear to be spaces in the tissue. There are many minute vessels in some of the sections having walls the cells of which stain deeply. The lumen of these vessels is not always uniform in size. Their general direction is away from the necrotic center. They seem to be lymph channels. The softened contents of the cavities are necrotic and have no structure. A few faintly stained nuclei and occasional normal nucleated cells are seen scattered throughout a granular eosin-staining field. There may be blue areas, which, with the high power, are shown to be aggregations of intensely staining bodies of irregular shapes and various sizes, presumably nuclear fragments. Between the necrotic and fibrous zones is a narrow zone, staining intensely with the basic stain. This also consists of nuclear fragments and homogenous blue-staining material. Contiguous to this necrobiotic zone, the fibrous tissue is embryonal in character, in which there may be small areas of degeneration and necrosis. As a rule the change from living to dead tissue is rather abrupt, as described above, but the transition may be much less clearly marked, and throughout the entire necrotic zone there may be nuclei which take the stain. In sections stained by Van Gieson's method for demonstrating connective tissue, the necrotic zone may give a picture resembling somewhat the arrangement of the fibers in the living tissue. Sections stained by Weigert's stain show elastic fibers in the more mature fibrous tissue. In sections stained with methylene blue or Gram-Weigert method the necrotic border of most of the cavities is seen to con-

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tain various bacteria, sometimes in enormous numbers. There may be bacilli of varying lengths, as well as branching threads and cocci singly, in pairs, groups or chains. In some of the growths all these forms are present; in others there are very few organisms. Usually the living tissue is free from bacteria, except in the margins of the necrotic zone, the organisms being most numerous in the necrotic layer upon the walls of the cavities. A small, slender bacillus or diplococcus is the most frequent organism observed. Filaments or threads are seen in sections from most of the growths. These threads either stain uniformly or appear as strings of deeply-staining spores or cocci in a less deeply-staining field. Cultures were taken from the necrotic material of a number of the growths with varying results. Usually from two to seven different organisms were isolated from each tumor. None of the organisms isolated were virulent enough to kill guinea-pigs. In a series of seven tumors a Gram-staining non-liquefying coccus was isolated twice, likewise a Gram-staining coccus which reduces glucose twice. A ray fungus was isolated from three different tumors of the series of seven. Smears from all the growths show threads, some of them branching. Anaërobic cultures gave no uniform results, all of the organisms isolated being facultative. From the morphologic standpoint the ray fungus is the most interesting organism isolated. It grows on all the ordinary media and on vegetable infusions. It grows best in the incubator, but will grow at room temperature. Each of the ray fungi isolated shows certain minor differences, such as the rapidity of growth on various media, and in the growth on potato, some of them failing to grow on potato; all liquefy gelatin and all stain by Gram's method. Swine were inoculated subcutaneously with pure cultures of the ray fungus, but the results were negative.

On Oct. 26, 1899, a 60-pound boar pig was inocu-

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lated by removing the right testicle, placing a small piece of necrotic material from tumor No. 5 of the series in the sac and sewing up the wound. The pig died November 20 and a necropsy made the following day. "There are no changes in the solid organs and other viscera except a moderate amount of hypostatic congestion of the lungs and some passive hyperemia of the liver and spleen. The apparent anemia of the organs is a striking feature. At the site of inoculation is a large indurated mass, which is removed. As excised, the dimensions are $20\times16\times10$ cm. The mass on section is seen to be made up of a central area of softening and discoloration and a surrounding capsule of dense scar tissue. The remaining testicle is partly within the area of necrosis, partly in the fibrous capsule, and a small portion external to the growth appearing normal. Histologically the changes already described are noted, viz., a central zone of necrosis and a zone of fibrous tissue. By the plate method a number of different organisms were isolated from this growth, but there were no colonies of the ray fungus. The query naturally arises, Is not the growth an ordinary abscess due to a mixed infection? A definite answer can not be given to the question at this stage of the work, but certain characteristics seem to point to the specific nature of it, viz.:

1. They never heal spontaneously.

2. Thorough drainage, such as is secured by a longitudinal incision carried deep enough to cut the tumor in two, does not result in a cure.

3. The peculiar manner in which the necrosis spreads regardless of lines of least resistance, as shown in the unremoved testicle of the pig inoculated with a portion of one of the growths, has already been stated.

October 8, 1900.

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THE GENERAL CHARACTERISTICS OF RAY FUNGI AND THEIR RELATION TO CERTAIN BACTERIA.

LUDVIG HEKTOEN.

The ray fungi are micro-organisms which have much in common with both the hyphomycetes and the bacteria. They resemble the former especially in growth and development; the latter especially in regard to some of the structural details, and also in the mode of action of the pathogenic forms.

Like the hyphomycetes, the typical ray fungi develop from small round spores, or conidia, into cylindrical threads, which branch and form a network.

The threads may be said to have an average thickness of half a micron; they do not contain any chlorophyll; originally they are homogeneous and solid, like many bacilli, and, as a general rule, they stain like the bacteria, retaining the color with Gram's method. Each single thread with its branches represents one whole, single organism.

From the surface of the mycelial layer arise hyphæ, or air threads, which by segmentation give rise to short chains of small round elements or conidia, which secure the propagation of the plant. The hyphæ are generally somewhat thicker than the mycelium.

In the older cultures the threads rapidly separate into shorter fragments which resemble spirilla, bacilli, and cocci, which in the typical ray fungi do not multiply as such, but, when transplanted, again grow into branching threads.

Kruse designates this later process fragmentation, and the formation of spores segmentation. The fragments and spores stain in the same manner as do the

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threads. In fragmentation the pieces, for a time at least, almost invisible within the thin, extremely delicate, almost invisible, external membrane, but eventually they are set free by the rupture of the membrane. Whether the sporelike bodies formed in the interior of the mycelium in connection with fragmentation are equivalent to the acrogenous spores has not been determined.

The importance of the formation of spores by segmentation in the propagation of the plants is shown by the fact that they develop in enormous numbers, covering the surface of the colonies with a white layer.

How far the spores are to be regarded as lasting forms similar to bacterial spores is a question. The spores are far more resistant to heat, to drying, and to other injurious substances than the threads. They do not exhibit any peculiar staining reactions, and there have been elaborated no procedures for double-staining of the spores and the threads, as in the case of the sporogenic bacteria.

In some otherwise typical ray fungi hyphæ develop but fail to give rise to spores (Actinomyces albido-fuscus asporogenes of Berestneff). Apparently such sterile hyphæ are white.

The majority of the ray fungi are aërobic and facultative anaërobic. A few are anaërobic.

The optimum temperature is 37° C. The actinomyces invulnerabilis of Acosta and Grande Rossi and the actinomyces thermophilus of Kedzior thrive at and resist high degrees of heat.

The majority are proteolytic, both in gelatin and in blood serum. Nearly all produce a peculiar moldy or earthy odor. Apparently the characteristic odor of freshly turned soil depends upon the presence of actinomyces odorifer of Rullmann.

While some produce no pigment, all sorts of more or less diffusible pigments are formed in the colonies of

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other varieties, and many varieties or species differ from each other only in the color of the pigment produced; most ray fungi produce one pigment, but polychrome ment formation, which is also favored by glycerin and varieties occur. Oxygen seems quite necessary for pigment formation, which is also favored by glycerin and glucose. In all the varieties the pigment is amorphous. except in the cases of actinomyces violaceus and rubidaureus, whose pigments are crystalline. The present division into species, introduced by Gasperini, rests largely on the pigment formation.

In general the colonies resemble those of some molds and to some extent the colonies of the tubercle bacillus. On solid media there develop tough, wrinkled, spherical growths, which send prolongations down into the substratum. The younger colonies are generally of a radiating or star-shaped appearance; hence the appropriateness of the word actinomyces, even though first used by Harz as descriptive of the granules which most of the pathogenic ray fungi form in the tissues. As the cultures become older or dry, the surface is generally covered by a white powder due to development of sporing air threads. In liquid media globules or ball-like masses are formed; the fluid remains clear. Many ray fungi also form a surface film, which eventually is covered by a layer of spore dust. Moisture, glycerin, and the absence of oxygen delay spore formation by hyphæ; in the absence of oxygen—spores are sometimes formed in the threads, as is the case with actinomyces albido-flavus when it grows in water. On surface growths small drops of oily fluid often appear. The hyphæ may be oily and hard to stain (Lachner), and Almquist points out that the oily exterior of the spores prevents wetting, and thus favors distribution by the air currents. In the cycle of development the different organisms classed as ray fungi touch each other so frequently that it seems quite correct to bring them together into one group.

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Ray fungi are abundant in Nature, occurring in the air, water and soil, and especially upon various grasses. They have been found in the mouth, pharynx, stomach, and intestines, upon the conjunctiva, skin, and in the vagina of healthy human beings, as well as to some extent in animals. In a hundred and eight examinations of human throats for diphtheria bacilli, Thiry encountered twenty-seven colonies of ray fungi. Upon ninety-four plates of agar and gelatin exposed to the air, Rossi-Doria obtained forty-nine colonies of ray fungi; as compared with the other organisms, about one colony of ray fungus occurred to every five hundred other colonies. The same number of colonies were obtained in the different seasons (Italy). In Rome he obtained about one colony to every two plates; in the woods and in a vineyard, about two colonies to every plate. In one plate exposed in the woods he obtained twelve colonies. He found actinomyces albus thirty-five times in forty-nine, actinomyces niger six times, actinomyces violaceus three times, actinomyces albido-flavus twice, actinomyces aurantiacus once, and actinomyces carneus once.

Undoubtedly the pathogenic forms are the result of adaptation to parasitism of ray fungi in Nature. The actinomyces albus has been isolated from air, grain, and water as well as from actinomycotic lesions. Lesions in the skin and mucous membranes open the door for the entrance of ray fungi upon the fragments of grasses and in the air, soil or water. Judging from the inoculation experiments with the typical ray fungi of actinomycosis with granules, there is good reason to believe that many of these organisms are slow to adapt themselves to new surroundings, and the comparative infrequency of actinomycosis indicates that the ray fungi, as a rule, find it difficult to acquire pathogenic powers.

The peculiar hyaline change in the membrane which leads to the formation of the characteristic clubs upon

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the surface of the granules formed in the tissues by many of the pathogenic varieties has long been emphasized, as well as the fact that the lesions are essentially chronic, characterized on the one hand by the production of granulation tissue with foci of suppuration, and on the other by the formation of nodular processes with caseation ("pseudo-tuberculosis"), while the production of virulent toxins seems of slight significance.

The ray fungi, by virtue of the characteristics just enumerated, are regarded by some as a family of the hyphomycetes; by others they are treated as a distinct group and placed midway, as the connecting link, between the hyphomycetes and schizomycetes. This is a botanical question which the pathologist is almost forced to consider because of questions of nomenclature and etiological classification of morbid processes.

While the majority of recent writers who have touched upon this question are content with one or other of the above propositions, others find reasons for a different classification. Thus Behla carefully reviews the previous efforts at classifying the organism of actinomycosis (in the old sense) and concludes that it is undoubtedly a thread fungus with true ramifications and hyphal spores. Behla proceeds upon the incorrect supposition that actinomycosis, even in the sense of Harz, is caused by a single species of ray fungus. Imbued with the idea that actinomyces in its pathogenic form is a developmental stage of some parasitic plant fungus, Behla undertook to study the parasites of barley.

In the course of his experiments Behla obtained actinomycelial vegetations upon bits of barley stubble, inserted under the oral mucous membrane of pigs, after having been covered with cladosporium and pleospora herbarum. The former is a common plant mold, occurring especially upon and beneath the epidermis of cereals, living or dead, as a thick, brownish-black covering, consisting of branching segmented threads with

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conidioferous hyphæ. When placed upon media of vegetable matter the conidia form threads, while in fluid media the threads do not produce conidia, but buds.

Cladosporium herbarum includes several species and is classed with the pyrenomycetes, a class of ascomycetes.

Behla regards the actinomycelial masses found in the tonsillar crypts of swine by Johne and others, often surrounding fragments of cereals, and by Ruge in human tonsils, but always without reactive changes, as approaching cladosporium in structure. He then goes a step farther and likens the bulbous expansions of ray fungi in tissues to conidia, regarding the branching of the clubs, the symmetric constrictions, and the apparent segmentation as supporting this already ancient view. The conidia of cladosporium, he assumes, lodge in some accidental lesion and form the mycelial network which under certain conditions develops conidioferous hyphæ.

According to this view, the ray fungi belong to the pyrenomycetes, but, unfortunately for this view, the structure of the ray fungi does not correspond with that of cladosporium, neither in the lesions nor in culture. Ray fungi have no septate threads, and the pathological and accidental nature of the clubs is taken for granted. The occurrence of ray fungi upon grasses, demonstrated by Berestneff, is a ready explanation of the development of actinomycelial vegetations in Behla's experiments.

For the present the ray fungi are best regarded as a distinct group, closely related to the simplest molds and to the bacteria. With the latter they are intimately connected by the bacillary forms and characters of the atypical and polymorphous ray fungi, as well as by the branching and club formation of certain rod-shaped organisms.

Whether the group of ray fungi is regarded as a family of the hyphomycetes, as advocated by Lachner, or is placed midway as the connecting link between the hyphomycetes and the schizomycetes, as urged by Kruse

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and Lubarsch with respect to the former streptothrices, is probably a matter of no special importance at this time.

The Atypical Ray Fungi.—The atypical ray fungi seem to form connecting links between the highest ray fungi and the nearest bacteria. The acid-proof ray fungi, such as actinomyces farcinicus, resemble the bacillus of tuberculosis not only in staining properties, but also very much in their special mode of pathogenic action. The polymorphous ray fungi, such as the actinomyces of Wolff and Israel, appear to have lost such characteristics of actinomycetes as spore formation, at the same time as they have taken on certian morphological and cultural peculiarities of bacteria, including in some cases the property of existing in the rod form and of mutiplying as such.

These transition forms on the part of the ray fungi are met, at is were, by certain organisms, now classed as bacteria, but which at times produce branching forms and under certain special conditions in the tissues some group themselves in masses with bulbous, hyaline projections. The bacilli—to use the old name—here referred to are the bacillus of tuberculosis and allied organisms, the bacillus of diphtheria, the glanders bacillus, and a few other less well-known organisms.

The Tubercle Germs.—The facts in regard to the organisms of tuberculosis and allied bacilli, so far as this point is concerned, are briefly the following: It has long been known that the bacillus of mammalian or human tuberculosis may occur in the form of branching filaments. Cornil and Babes figured ramifications in 1883. A. Petrone, in 1884, found branching forms in the exudate of tuberculous leptomeningitis and called attention to the fact that on this account the tubercle germ should be placed between the "micromycetes and schizomycetes."

Nocard and Roux, Metchnikoff and Klein found

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branching and filamentous forms. Metchnikoff advanced the opinion that the tubercle bacillus represented a stage in the development of a thread fungus and proposed the name sclerothrix kochii. Klein looked upon the branching as a reversion to an ancestral type presenting mycelial growth.

Johan Olsen regards most bacteria as adaptation forms and not as true, independent species. They are in reality imperfect and imperfectly known fungi. Parasitic adaptation may be closely associated with pleomorphism. The ray fungi are genuine mycelial fungi which pass by various stages into bacilli, and the tuberculomyces is a ray fungus or streptothrix because it has branches.

In 1893 Fischel described threadlike, branching, and bulbous forms in the colonies and called especial attention to the great similarity in the appearance of the colonies of the tubercle organism and of actinomyces hominis.

Coppen-Jones also described threadlike and branching forms of tubercle bacilli in the sputum and in the pure cultures. He furthermore made it appear probable that this organism may present a type of spore formation which is homologous with chlamydospore formation of certain true molds, such as mucor. For these reasons Coppen-Jones regarded it as imperative that the tubercle germ be removed from the bacteria proper, and proposed the name tuberculomyces to indicate its true nature.

McWeeney, Semmer, Bruns, Babes, Marpmann and Craig all describe branching and filamentous forms of tubercle bacilli, either in sputum or in cultures.

In 1892 Maffucci demonstrated that the bacillus of avian tuberculosis also grew in branching forms. Indeed, it seems probable that it was this organism upon which Metchnikoff made the observation already referred to. Lubarsch has made the observation that when

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cultures of the bacillus of avian tuberculosis, after standing in a dark place for some time, are again placed in the incubator, typical branching forms and greatly thickened bacilli occur very numerously.

For a long time the tubercle bacillus was supposed to stand quite alone, a typical bacillus presenting at the very utmost but two varieties, the avian and the human. Of late it has been found, however, that the hitherto apparently so unchangeable and strictly parasitic tubercle bacillus may receive profound modifications when passed through the bodies of cold-blooded animals, such as the frog, etc., and furthermore that organisms resembling it closely occur freely in Nature. The similarity between the acid-proof atypical ray fungi and the tubercle bacilli has already been noted.

It has been shown by Bataillon and Terre and by Möller that when the bacillus of human tuberculosis is passed through the bodies of frogs and lizards it becomes so modified that it adapts itself much better to a purely saprophytic existence than before. The growth on artificial media is more luxuriant, takes place at ordinary temperature, and its virulence is materially altered. Under these conditions, which are regarded by Lubarsch as representing something of a reversion to its original saprophytic existence, the branching is more frequent, regular and pronounced. Granular and irregularly swollen forms also occur oftener.

From timothy and cow dung Möller isolated three closely related but distinct bacilli, which resemble tubercle bacilli in morphological, pathogenic, and many cultural properties. Möller's timothy or grass bacilli, as well as the similar organism isolated from butter by Petrie and by Lydia Rabinovitch, form granules, button- and club-shaped swellings, as well as branching threads, upon some or all media, and to a greater or less extent.

Babes and Levaditi were the first (1897) to describe an actinomycelial arrangement and form of tubercle

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bacilli in tissues. When pure cultures of slight virulence were injected between the dura and the pia mater of rabbits there developed in a few days undulating filaments, often in masses, which in eight or ten days presented radiating peripheral ends and later acquired nodular thickenings and even distinct clubs. Such masses at times greatly resembled the granules of actinomycosis. Ehrlich's and Gram's stain showed a central mass of bacilli, and aniline-saffranine, followed by Lugol's solution, stained the bulbous or clubbed ends red. In many cases bacilli were seen to end in clubs.

Soon afterward Friedrich reported similar results of an independent investigation. He injected suspensions of tubercle bacilli in physiological salt solution into the left ventricle through the carotid artery of rabbits. Death usually resulted in from twenty-four to eighty-six days. On staining sections of tubercles in various organs, such as the iris, the kidney and the brain with Victoria blue and differentiating with alkalies, there would be found masses of bacilli, surrounded by radially arranged actinomycelioid clubs and bulbs.

Schulze confirmed the results of Babes and Levaditi and of Friedrich in the more important details. He found that tubercle bacilli from various sources and of varying virulence would arrange themselves in radiating foci and assume the form of metachromatic clubs and other irregular shapes, both when injected into the arteries and when implanted directly into the brain, kidney, liver, testicle and mammary gland. The animal used was the rabbit, and the actinomycelioid masses, which in no case appeared before the fourteenth day, formed earliest in the case of the cultures of least virulence. The Gram-Weigert staining method was found to bring out best the early clubs, which the Ziehl-Neelsen's method failed to show at all; in some cases the clubs had a special affinity for acid stains, in others for basic, their staining reactions being uncertain. The

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larger clubs were refractile and insoluble in alcohol, water, alkalies and acids.

Schulze also found that the fungus of avian tuberculosis and actinomyces eppingeri would arrange themselves in masses with club-shaped prolongations when injected under similar conditions as those mentioned. In the case of actinomyces eppingeri Birch-Hirschfeld's stain colored the threads blue and the clubs red.

Schulze demonstrates, by obtaining from the resulting foci pure cultures only of the organisms injected, that in all likelihood no weight can be attached to Boström's criticism to the effect that the appearances described by Babes and Levaditi, Friedrich and Lubarsch were due to molds introduced at the same time as the tubercle bacilli. Schulze regards the formation of clubs as pathological and due principally to the hindrance of the growth of the organism on account of the hostile influence of the surrounding cells. This is indicated by the observation that ray forms are most numerous and most regular in localized tuberculous proliferations, as occur especially in the brain and the kidney; there is always a close relation between the fungi and the cells, the organism lying either in mighty giant cells or closely surrounded by giant cells or leucocytes. The formation of ray foci occurs also in the case of pathogenic molds, such as aspergillus and mucor forms, under similar circumstances, as shown by Ribbert and Lichtheim, and I have observed it in the case of aspergillus fumigatus.

Lubarsch, in whose laboratory Schulze carried on his studies, investigated a number of other related organisms in regard to their forming ray foci under certain circumstances. He corroborates Schultze's observations as to the bacillus of avian tuberculosis and the actinomyces of Eppinger.

Tubercle bacilli (human) modified in the direction of a more vigorous saprophytic existence by passage

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through frogs, as demonstrated by Bataillon and Terre, or by a sojourn in the body of lizards, as pointed out by Möller, produced in rabbits caseous and round-cell foci containing but few radiating masses of bacilli, the majority of which seemed to be undergoing disintegration. The bacillus of fish tuberculosis, isolated by Bataillon, Dubard and Terre, and believed by these authors as well as by Möller and Lubarsch to be a modified form of tubercle bacillus, did not multiply in the rabbit's brain or kidney, and did not produce ray foci.

The acid- and alcohol-proof bacilli isolated by Möller from grass and dung (Möller's timothy bacillus I and II, Möller's cow-dung bacillus) and by Lydia Rabinovitch from Berlin butter (Rabinovitch's butter bacillus) were all found to produce clubbed ray foci when implanted in the tissues. In some instances bacilli could be seen in the interior of the clubs. These organisms form irregular thickenings and also true branches in artificial cultures. Lubarsch obtained the most satisfactory results with Möller's timothy bacillus No. I; local as well as intra-arterial inoculation was followed by the formation of small, short, pointed clubs, which soon increased in size at the expense of the central part, so that the whole mass became metachromatic and acidophilous, and granules visible to the unaided eye were formed; the nodules which developed around the ray foci resembled so much the typical tubercle that in rabbits the lesions caused by the timothy bacillus are not distinguishable microscopically from those caused by the tubercle bacillus.

Lubarsch could not obtain actinomycelioid masses with the bacillus of glanders, which Semmer, Marx and others have shown produces true branches, neither with the bacillus of diphtheria nor with two varieties of ray fungus isolated by Petruschky, but not fully described. The diphtheria bacilli and Petruschky's fungi did not multiply in the tissues, while the glanders bacillus,

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however, spread more diffusely through the resulting nodule.

The club formation on the part of tubercle bacilli and allied organisms, when deposited in the tissues under certain circumstances, is regarded by Lubarsch, as in the case of some of the fungi of actinomycosis, to depend upon a hyaline swelling of the membrane of the organisms, because in not a few instances rods or threads could be followed into the clubs as axial filaments.

Lubarsch holds with Schulze that the clubs represent malformations, the result of hindrance to growth (hemmungsmissbildung), rather than purely degenerative changes, because the clubs develop only when the organisms injected multiply *in loco* and not when direct disintegration takes place. Lubarsch believes that the club-shaped thickenings of actinomycelial clusters also have the same general significance.

In connection with this it may be mentioned that in the contents of phthisical cavities Coppen-Jones found formations absolutely identical in shape and form with the clubs and bulbs of actinomycelial granules. He concludes, however, that the objects were not the result of changes in organisms, but due to colloid or other deposits upon elastic fibers and other organic remnants.

The Branching of Diphtheria, Glanders and Other Bacilli.—Branching diphtheria bacilli have been described by a number of authors (Klein, Bernheim and Folger, Meyerhof, Hill, *et al.*). Apparently such forms are not uncommon. The form most frequently assumed by the branched bacilli observed by Hill was that of a tri-radiate star. The branching forms frequently presented a granule, in every way similar to the ordinary granules of diphtheria bacilli, situated at the point where the branches originate.

Semmer, E. Levy, and Hugo Marx describe branching forms of the glanders bacilli. Marx, especially,

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found longer and shorter branching threads, especially in older cultures.

Babes, E. Levy and others describe branching bacilli in connection with leprosy. Stolz, Löffler and Koch also record the observation of branching bacilli under various circumstances.[1]

As already noted, Lubarsch failed to obtain clubbed granules in the tissues with the bacilli of diphtheria and glanders.

There has not been entire unanimity as to the interpretation and significance of the branching forms of the various bacilli mentioned.

A. Fischer regards them as involutional, of a pathological and degenerative nature, consequently without any phylogenetic significance. Most investigators, however, hold that these organisms are not true bacteria, but growth forms of higher fungi.

In the light of the studies of Fischel and Coppen-Jones, Hueppe regards the tubercle bacillus as a parasitic growth form of a pleomorphic mold.

For morphological reasons principally the branching bacilli are generally regarded as closely related to, if not identical with, the ray fungi (Fischel, Johan Olsen, Coppen-Jones, Kruse, Lachner, Schulze, Lubarsch, Hill, etc.).[2]

Lubarsch proposes to include under the group name of streptothrix all the ray fungi and also those organ-

1. In the Centralblatt für Bacteriologie, vol. xxii, 1897, Kitt described a streptothrix form of the rothlauf bacillus. In a correction in vol. xxiii, of the Centralblatt, 1898, he states that he has subsequently found that there existed a very close symbiosis between the rothlauf bacillus and a distinct streptothrix. In his original communication he called attention to the fact that on gelatin only the rothlauf bacillus appeared, whereas on transplantation from gelatin to slanting agar and bouillon the streptothrix form appeared, but no colonies of bacilli. Subsequently he found, however, that the bacilli grew under the colonies of the streptothrix, and that when transplanted into gelatin the bacilli surpassed the streptothrix in growth. This symbiosis continued throughout six months.

2. From his study of the structure and development of the colonies of the bacillus of tuberculosis, Ledoux-Lebard concludes that

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isms, usually classed as bacteria, which occasionally produce true branches in the cultures and ray forms in the animal organism. He would place this group midway between the hyphomycetes and the schizomycetes, because its members represent transition stages between the higher and the lower fungi. Thus the streptothrices with branching mycelium and distinct spores are so closely related to the hyphomycetes that by many they are made a distinct family of the thread fungi. The tuberculomyces and allied organisms, on the other hand, are probably parasitic adaptation forms of similar fungi, which have largely or wholly lost the power of branching and spore formation, and on this account resemble the fission fungi. Lubarsch would further create a distinct family in the streptothrix group of those organisms which appear in ray form in the tissues. To this family he would apply the distinctive name of ray fungi.

I do not believe that this proposition is well considered. In the first place, there are objections to the use of the word streptothrix in this connection. In the second place, the carrying out of this proposal would throw together in a closed circle the most typical of this group, such as actinomyces albus, with the most atypical or imperfect, such as the tuberculomyces, to use the word suggested by Johan Olsen and Coppen-Jones, simply upon the strength of a pathological manifestation—namely, that of club formation—which in the case of the tubercle fungus is apparently of extreme rarity because of the special conditions required for its development.

there is just as much reason for placing this organism in the genus cladothrix as in the ray-fungus group, if not more. The typical cladothrix is a sheathed filamentous organism with false ramification, and each ramified cladothrix is a colony like any zoogloea, whereas a ray fungus with its true branchings is one and the same individual. In their growth Ledoux-Lebard found that Koch's bacillus as well as the avian group themselves grew after the type of cladothrix—*i. e.*, as ramifying segmented filaments.

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The demonstration that tuberculomyces may form ray foci is undoubtedly important, because it brings further proof of the relationship of this organism to the ray fungi, but for the present these observations are hardly sufficient to form the basis of the ultimate classification of organisms of whose natural history but very little is as yet known.

As a matter of fact, the tuberculomyces and other allied organisms resemble much more the acid-proof and atypical ray fungi, which do not form actinomycelial clusters in the lesions of spontaneous actinomycosis, than they resemble the typical pathogenic ray fungi. Consequently it would appear more natural to place the tuberculomycetes in the subgroup of the atypical, acid-proof ray fungi. As regards the remaining bacilli which occasionally produce branches (bacillus diphtheriæ, glanders, etc.), the observations at hand simply indicate that they resemble in many respects the polymorphous atypical ray fungi, not having been shown, however, to form clubbed granules in the tissues.

The foregoing considerations demonstrate clearly, as emphasized by Hueppe, that the usual designations bacilli, bacteria and bacteriological are not adequate to represent "correctly and scientifically the exact situation." Of the various terms already proposed as substitutes for the old name, the bacillus of tuberculosis, such as sclerothrix Kochii (Metchnikoff), mycobacterium tuberculosis (Marpmann), the at present most available and probably most significant would be tuberculomyces, the tubercle fungus, the fungus of tuberculosis.

Should the observations ultimately make it clear that the diphtheria bacillus also belongs to the ray fungi, then the substitution of fungus for bacillus would indicate its botanical position more clearly.

As pointed out by Hill, the interest which attaches to the demonstration that certain bacilli—i. e., organ-

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isms consisting, by definition, of unbranched cells or chains of cells—occasionally show individuals which branch very distinctly, is purely morphological and botanical. Elementary definitions may be affected, but accepted beliefs concerning the etiological relations of these organisms to pathological conditions remain unchanged.

October 12, 1899.

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REPORT OF THE HISTOLOGIC CHANGES FOUND IN THE TISSUES OF ANIMALS INOCULATED WITH THE DIPLOCOCCUS SCARLATINÆ (CLASS).

E. R. LE COUNT.

The animals inoculated by Dr. Class with pure cultures of diplococcus scarlatinæ include three pigs (swine) of which two were inoculated intravenously and one into the peritoneal cavity; one died at the end

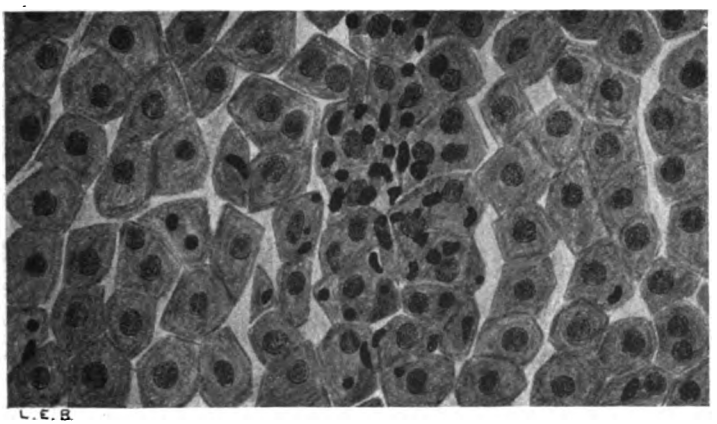

Fig. 1.—Area of necrosis in liver of a guinea-pig with leucocytic accumulation. (Iron-hæmatoxylin staining.)

of a week, and two were killed on the thirteenth and fourteenth days respectively; three guinea-pigs inoculated in the peritoneal cavity died on the fourth, fourteenth and seventeenth days. The organs of these animals were examined as well as those from a number of mice. Death took place in these last-named animals very quickly and the organs show practically no changes. Pure cultures of the diplococcus were obtained from the heart's blood and different viscera in every case.

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Bacteria were not found in any of the sections. It is possible that the diplococcus, which is polymorphous, could not be distinguished from chromatic granules.

In larger animals very definite changes are present in the larger animals very definite changes are present in certain organs. In the livers of the pigs are focal necroses that are, however, always small; they occupy but a small part of the lobule and contain fibrin. The necrotic liver cells are replaced by accumulations of cells which are evidently leucocytes and many of them

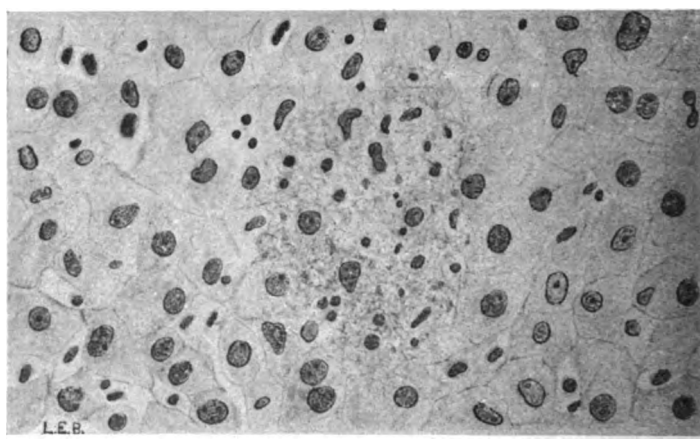

Fig. 2.—Area of necrosis in the liver of a pig with fibrin formation. (Weigert's fibrin staining.)

eosinophilous; in these accumulations a few cells are present that resemble plasma cells in morphology and staining reactions.

Often the clumps of cells within the capillaries block the channel without any observable changes in the adjacent liver cells; in places these accumulations are most marked near the central vein. Nuclei in karyokinesis occur in the endothelial cells lining the capillaries within lobules and in leucocytes. Very few cell inclusions occur.

In the liver sections of guinea-pigs similar changes

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are present. Many eosinophilous cells, a few cells resembling plasma cells, cells with pyknotic nuclei and small amounts of fibrin are found in the capillaries and small focal necroses of the liver tissue. In the Malpighian corpuscles of the spleens from swine, dividing nuclei occur as well as occasional free chromatin granules. There are no necroses in the spleen, and such masses of fibrin as occur are in small vessels and have every appearance of postmortem clots. In the spleens of guinea-pigs similar changes occur; plasma cells are very abundant in some sinuses; phagocytic cells or cell inclusions are not rare, plasma cells often fill the sinus.

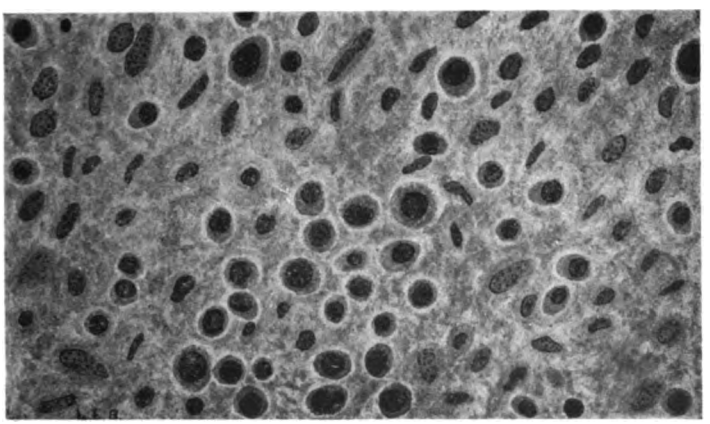

Fig. 3.—Cluster of large plasma cells in a sinus of the spleen of a guinea-pig. (Polychrome blue and eosin staining.)

The lymph glands from the swine show no histological changes that can be considered abnormal, with the exception of enlarged nodules, lymph sinuses that are packed with cells, an abundance of multiplying cells in the germinal centers, and in one animal small amounts of fibrin within the sinuses. In the kidneys of the swine, the only change is swelling of the epithelium, and this is not marked; in the kidneys from the guinea-pigs, the epithelial swelling is more marked and a few

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hyaline casts occur. The other organs examined, viz., the lungs, heart, stomach, intestines, thymus and bone marrow show no changes. In the adrenal of a guinea-pig beautiful minute focal necroses occur similar to those in the liver, and in the skin of a pig the seat of a rash, engorgement of the blood vessels is present.

It is obviously of doubtful value to compare the histologic changes in these few animals with the elaborate study by Pearce[1] of the minute anatomy of human scarlatina; yet it is evident that these changes here reported differ from the alterations described by Pearce in degree rather than character. One chief difference is in the lack of lesions in the kidneys in the animals in comparison to the changes in this organ in scarlatina. There is a similarity in hyperplasia of lymphoid tissue, focal necroses, and the occurrence of plasma cells in situations that betoken their presence in the circulating blood.

January 14, 1901.

AN EXPERIMENTAL STUDY OF THE ORIGIN OF THE EPIDEMIC OF TETANUS FOLLOWING JULY 4, 1899: REPORT OF CASE, WITH RECOVERY.

H. GIDEON WELLS.

In the wake of the last celebration of Independence Day there occurred throughout the country an epidemic of tetanus. Judging from the newspaper records the mortality was high, even for traumatic tetanus, but the

1. Medical and Surgical Reports of Boston City Hospital, 1899, xl, 39-82, and Journal Boston Society Medical Sciences, vol. iii, p. 161.

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most striking feature was the identity of the cause, i. e., wounds from blank cartridges. One of these cases was in my care at the Cook County Hospital in the service of Dr. George F. Butler, and was the only one of five cases, occurring at the same time, to recover. All were due to wounds made by blank cartridges, in three the left hand being injured. Two of the other cases were in the County Hospital, each dying shortly after admission. The other two were in the private practice of Chicago physicians. Other cases may have occurred in the city, but I do not know of them. The history of this case is as follows:

L. O., a Norwegian laborer, aged 40 years, was shot above the left knee on July 4, by a revolver loaded with blank cartridges. He always refused to tell how he was injured or by whom. The wound became infected and caused him so much pain that he entered the hospital on July 14. Up to that time he had no constitutional symptoms. On July 15, Dr. C. J. Rowan, house surgeon, observed that the patient could not open his mouth readily and that there was much rigidity of the lower jaw, and transferred the patient to the medical service. The patient said that he had first noticed the stiffness in his jaw on the preceding day, ten days after receiving the injury.

When admitted to the medical ward the patient's temperature was normal, and no rigidity could be observed except in the lower jaw. A slight risus was present. The wound was located on the anterior surface of the left thigh, six inches above the patella. About it was some induration, and a sinus led downward nearly to the upper end of the reflection of the synovial sac beneath the quadriceps extensor. From the wound pus exuded, and stained specimens showed myriads of bacteria of many sizes and forms, a few of them being sporulated. There was no lymphangitis or adenitis.

Chloroform was administered and under surgical asep-

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sis all the tissue within one-half inch of the wound surface was removed. After this the entire wound was cauterized with Paquelin cautery, every portion of the surface being gone over twice, so that the tissue was killed for a considerable depth. This was done with the greatest possible thoroughness, nearly two hours being spent in the excision and cauterization. Two pasteboard wads were found at the bottom of the sinus, and from them as well as from the pus, the tetanus bacillus was isolated by Kitasato's method.

Ten cubic centimeters of tetanus antitoxin was injected, and this was repeated twice, 24 hours apart, 30 c.cm. in all. Quiet was secured by placing the patient in a darkened room with the floor thickly covered with blankets. Chloral hydrate and sodium bromid were given regularly, and morphin sulphate was given hypodermically as often as was necessary to keep the patient drowsy. On the second day the temperature rose to 100, and remained near this point for nearly two weeks, only once reaching 101. The day after the operation the trismus became more marked, and there was much rigidity of the muscles of the trunk. On the following day, attacks of orthotonus began to develop, and these were repeated for about a week whenever the patient was disturbed. The jaws became almost completely immovable on the second day. Two days later they relaxed slightly and improved steadily thereafter, but stiffness was not entirely gone until three weeks later. A mild delirium began soon after the trismus set in, and lasted for about two weeks, despite the administration of sedatives. Except for this there were no complications.

Especial care was taken with the articles coming in contact with the wound or with the patient. Such articles, where possible, were burned. the remainder were soaked for 24 hours in 1 to 500 bichlorid solution, with ½ per cent. hydrochloric acid, the acid greatly lessen-

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ing the resistance of the tetanus bacillus against germicides.

Carbolic acid treatment was suggested and a few doses were given late in the case, but too near the approach of convalescence to estimate its effect. It is impossible to say that the antitoxin was or was not of value. Every feature of the case was in favor of a good prognosis. The long period of incubation, ten days, the absence of high temperature, and the mildness of the spasms, all gave a hopeful outlook. How much of this was due to the earliness and thoroughness of the removal of the infected tissue is also conjectural, but I believe that the mildness of the attack is to be credited to this part of the treatment.

That so large a proportion of the tetanus in this epidemic followed wounds by blank cartridges suggested the possibility that the cartridges contained tetanus bacilli or spores. Accordingly, a thorough study has been made of blank cartridges that were on the market at that time, the work being done in the laboratory of pathology of Rush Medical College. Inquiry showed that they were manufactured by five different firms in this country and Canada, and samples of each of these makes were obtained. In all, about 200 cartridges have been examined, but invariably with negative results.

Cultural and inoculation experiments were made as follows: First, the wads, powder and shells were cultivated by Kitasato's method for isolating the tetanus bacillus, i. e., a preliminary heating at 85° C. for 45 minutes to kill off all but resisting spores, such as those of tetanus. Glucose-agar was generally used, but bouillon, glycerin-agar and gelatin were tried. These cultures failing to show the organisms sought, cultures were made without the preliminary application of heat, with the same results. A series of inoculations of guinea-pigs and house mice followed. Some deaths from pus infection resulted, but the tetanus bacillus could never be

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found. The inoculations were made in various series with wads, powder, agar and bouillon cultures, with and without preliminary heating. Ultimately, in order to examine large numbers of cartridges the following plan was adopted: Wads from ten cartridges were broken into fine pieces and placed in bouillon sufficient to cover them, the cultures heated to 80 to 85 C. for 45 minutes, and grown for one week. The cultures were then inoculated into mice or guinea-pigs, and stained specimens examined. All cultures were, of course, made anaërobically. Agar-cultures were made in deep stabs; the bouillon was boiled to remove air, and after inoculation covered with a layer of paraffin. The tubes were then placed in sealed jars with an alkaline pyrogallic acid solution to deoxygenate the atmosphere.

Considering the possibility of the bacilli being present, but of weakened virulence, wads were implanted into the muscular tissue of animals and allowed to remain there for periods of three days to two weeks. They were then removed and inoculated into other animals or cultivated anaërobically, with the usual negative result.

Several anaërobic organisms that survived the heating process were found, and at times caused confusion. One of them that occurred constantly in one make and occasionally in another, was quite similar in some respects to the tetanus bacillus. It was a long bacillus, slightly larger in all ways than tetanus, with a spore which was usually at one end, sometimes in the center. This spore, however, was slightly oval so that the typical pinhead form was not exactly duplicated. Organisms from fresh cultures stained by Gram's method, but lost that character as the cultures became older. They seemed to have a slight motility. When grown in glucose agar they produced much gas which had the odor of decomposing cheese, quite different from the "burnt garlic" odor of tetanus. They were obligate anaërobes

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and could only occasionally be made to grow on the surface of slant media even in a deoxygenated atmosphere. Inoculations into mice and guinea-pigs showed this organism to be non-pathogenic—10 c.c. of a week-old bouillon culture injected into a guinea-pig seemed not to affect the animal in the least.

These investigations have failed to show that the origin of the infection is attributable to the blank cartridges. It is fully appreciated, likewise, that this origin is not absolutely excluded. It is, of course, possible that other samples might give different results, yet the manufacture of these articles is such that each one represents quite exactly the composition of all others, the materials being made in large quantities and under fairly constant conditions. Microscopic examination of the wads shows them to be made of wood pulp. It was thought that straw might be one of the ingredients, giving a possible direct source of contamination, and in one make some particles that seemed to be straw fragments were mixed with the wood pulp.

The occurrence of so many cases of tetanus from a common cause was ground for a strong suspicion that the germs were to be found in that cause, so a negative result was by no means expected when this investigation was started. No report of a similar study of this recent epidemic has been found in the medical literature for the past year, hence these results are submitted.

June 11, 1900.

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TWO CASES OF EMPHYSEMATOUS GANGRENE, CAUSED BY BACILLUS AEROGENES CAPSULATUS.

L. M. LOEB.

CASE 1.—A cooper, age 43, was admitted to the Cook County Hospital December 30, 1900; service of Dr. Hartman. Five days previously he was seized with a sudden pain in the left shoulder. On the following day his arm began to get red and swell. On the third day a papule appeared on the outer side of the arm over the lower part of the deltoid. This enlarged gradually in spite of poultices. Patient was sure that he had not injured the hand or arm and that the skin was not broken at any point. He had coughed for three years and expectorated a purulent material, but no blood. Examination on admission shows:

Lungs.—Râles over large part of chest; breath sounds are faint, and there is considerable dulness over lower posterior portion on both sides. The breath is very offensive.

Left arm, shoulder and upper portion of forearm are edematous and very tender. Over the deltoid is an ulcer surrounded by an area of emphysema extending down over the clavicle in front. There is a very offensive odor to the sore.

Treatment consisted of free incisions through the ulcer. A large amount of pus was liberated. The odor was very foul. The wound was irrigated with 1 to 500 bichlorid and an iodoform gauze drain was inserted. Hot boric dressings were applied.

The patient became worse and the edema rapidly extended, finally involving the whole face, scalp and chest. Later emphysema was detected in this whole

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area, and the tissues contained a foul-smelling pus. The temperature was remittent in character, pulse corresponding. Patient died 24 days after admission to the hospital.

At the autopsy by Dr. Wells were found:

Emphysema and edema of the entire body. Under the scalp was a layer of pus one-half inch thick. The muscles of the arm about the wound were cloudy and opaque, but contained no pus. The marrow of the bones was soft and fluent.

Consolidation of right and left lower lobes of lungs—chronic tuberculosis and edema of lungs.

Parenchymatous degeneration of heart muscle, liver, spleen and kidneys.

The anterior mediastinum, heart's blood and bile contained gas.

Bacteriologic Examination (Mr. Ohlmacher).—The bacillus aerogenes capsulatus was not found in smears or cultures of the heart's blood, but it was found after inoculation of heart's blood into rabbits, which were killed and in 24 hours presented the characteristic lesions. An organism corresponding morphologically and tinctorially with the gas bacillus was found in the heart muscle, lung, kidney and liver. In all of these, gas bubbles were also found on microscopic examination. Cultures from the heart's blood showed staphylococcus aureus, streptococcus pyogenes and the colon bacillus.

This case is peculiar in the absence of the usual traumatic history. Of nontraumatic cases only 5 had been reported to July, 1900 (Welch).[1] Of these 1 followed erysipelas, 2 gangrene (whose nature is not stated), and for 2 no explanation has been given.

Case 2.—Charles H., aged 9, was admitted to the Cook County Hospital June 3, 1900, service of Dr. J. B. Murphy. On the preceding day he tried to jump on the rear end of a wagon, but fell, the rear wheel just grazing his leg. This happened at noon. A physician attended

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him and cleaned the wound. At midnight the mother noticed that the child was delirious, and her physician advised that he be taken to a hospital.

On examination no changes were found, except at the site of injury. The child was delirious. On the evening of admission his temperature was 104°, pulse 152, respirations 48. The wound consisted of an abrasion at the outer aspect of the knee, brownish in color, and of the size of a dollar. There was a red linear streak, passing from this point two-thirds of the way to the ankle. The wound was cleaned and dressed with 1 to 1000 bichlorid.

On the following day a small sinus was noted in the lower angle of the wound. From this a brownish serous fluid could be expressed, which contained a rather large amount of gas. No foul odor to the fluid was noted. A probe was introduced into the sinus; it passed easily for its whole length in a downward direction. Crepitation could be felt as far down as the external malleolus. The tissues were very pulpy and yielded readily to the slight pressure of the probe. Amputation was advised and absolutely refused. In place of it 15 to 20 longitudinal incisions 2 to 3 cm. long were made on the outer and posterior aspects of the leg. On the seventh day several sloughing tendons protruded through one of the incisions just above the ankle. They were drawn out and tore off readily. By the tenth day all of the skin of the external and posterior aspects of the leg had sloughed.

During all this time, patient gave evidence of a profound intoxication, as high temperature, rapid feeble pulse, delirium and rapid emaciation. Ten days after admission no more gas was noted in the exudate, but the pus became thicker and yellowish. The case was complicated by a suppurative synovitis of the knee-joint, which yielded readily to treatment, but left the knee in such a position (subluxation backward) that a resection was deemed necessary later on.

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Specimens from the case were studied by Mr. Dunn in Dr. Hektoen's laboratory. His report is as follows:

June 4, 1900. Smears from the pus showed staphylococci and streptococci in small numbers, and a large, rather thick bacillus from 4 to 7 units in length. This organism retained the stain by Gram's method poorly. It stained either entirely or showed a number of more or less irregularly staining granules, which closely resembled streptococci. Anaërobic cultures were made in jars deoxygenated by an alkaline solution of pyrogallic acid. In 24 hours marked growths were visible. The agar in which the cultures were made was full of gas bubbles, and there was a small amount of liquefaction in the neighborhood of the colonies. In some of the tubes there was a distinct stratum of gas 2 to 4 cm. in thickness. Smears from the cultures showed an organism comparable to the one above described, but if anything more easily decolorized by Gram's method. The bacillus was very sluggish if at all motile. About 3 c.c. of a bouillon culture was injected intravenously into the ear of a rabbit, and after 3 or 4 minutes the animal was killed and incubated for 24 hours. On removal from the incubator the animal was puffed up to twice its normal size, and emitted a foul odor. The subcutaneous tissue was emphysematous, and a typical "Schaumleber" was present. Smears from several of the organs showed the same organism. This germ stained distinctly by Gram's method, and was encapsulated. Cultures presented the characteristics above mentioned, and the bacillus stained irregularly, but not so much so as that in the first culture. Two c.c. of bouillon culture were injected subcutaneously into a guinea-pig, but the animal is now in apparent good health.

In pus from the same source two weeks later none of the bacilli could be found. In tissue obtained from the wound at the same time, the organism could not be satisfactorily demonstrated. In the tissue there is marked

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formation of connective tissue, leukocytic infiltration and endarteritis. In one piece of tissue there is much fat with a few irregular vacuoles that may be due to gas. Some of the cells show fatty degeneration.

The symptoms presented are similar in all respects to those often described in recent years as associated with infection by the bacillus ærogenes capsulatus, accompanied and followed by the ordinary pus organisms. The manifestations were, however, in the second case unusually severe even for one of these cases when the injury itself was so slight. The rapid extension of the emphysema, together with the profound intoxication, point to great virulence in the bacteria.

Since the first description of the bacillus by Welch and Nuttall[2] and Fränkel's[3] independent investigation, much interest has been aroused in this organism. Fränkel isolated the bacillus from three cases of phlegmonous emphysema and was the first to establish the relationship of this lesion and the gas bacillus. Since Fränkel's and Welch's papers, practically all cases of gas formation in the tissues during life or immediately after death have been shown to be due to the bacillus ærogenes. "The bacillus ærogenes capsulatus or bacillus Welchii practically dominates the whole field of pneumatopathology." It has been found that the bacillus of malignant edema rarely, if ever, produces those lesions, which were always attributed to it.

The virulence of the organism has been shown both clinically and experimentally to vary greatly. In healthy tissue it gains a foothold with difficulty. Frequently not until the death of the patient or of the tissue does it produce gas. It has been found in mild infections, which have been cured spontaneously. In fact, even in virulent cases, should the patient live, the bacillus usually dies off within two weeks. Although the intestine appears to be one of its habitats, it rarely becomes active there except in cases of typhoid perforation.

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appendicitis or strangulation. The variation in its action is well shown by contrasting three cases reported by Menge and Krönig[4] with one of Dobbins.[5] In the former, fetus and placenta were emphysematous, but the puerperium was normal. In the latter, in spite of an early diagnosis and active treatment, emphysema rapidly became generalized and death ensued in a few days.

Altogether about 60 cases of emphysematous gangrene due to the gas bacillus have been reported. Of these about one-half terminated fatally. Of the other half in the large majority of cases, either the symptoms were mild throughout or recovery followed an early amputation of the limb. Mann,[6] in 1894, reported the first case in which a cure took place without this radical procedure. Free incision and a continuous bath, as in his case, seem ample when the affection is rather superficial and accessible, but with complications, such as compound fractures, where every portion of the wound can not be reached by air, amputation alone offers any hope in checking the progress of the infection.

Fränkel, as early as in his first paper, drawing his conclusions from experiments on lower animals, stated that cure is hastened by an early incision of the inflamed parts. Wherever an early diagnosis is made of the infection—and all agree that this is essential for its successful treatment—incisions should be made to expose all parts affected. Bloodgood,[7] after a review of numerous cases, says: "When the wound is opened and left open, the danger of infection from the organism is not great," but that if the symptoms are not relieved immediately by free incisions and the bath treatment, amputation is indicated.

The survival of the second case with a useful, though mutilated extremity, points to a further consideration of conservative measures. Often, perhaps, when the infection is not too deep, with free ventilation and

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repeated incisions, where there is progressive involvement, the infection might gradually become limited and finally yield. How much the great mortality has been due to insufficient opening of the parts can not be said. Many more reports of cases must be had to determine the best way of combating this infection.

April 8, 1901.

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THE OCCURRENCE OF TYPHOID BACILLI IN THE URINE OF TYPHOID PATIENTS.

HOWELL E. DAVIES.

I may summarize my results as follows:

1. Out of 418 specimens of urine, representing 65 cases of typhoid fever, 105 specimens, representing 21 cases, showed the presence of the typical typhoid bacillus.

2. In 47 specimens representing 14 cases, were found bacilli that resembled the bacillus of typhoid fever in some respects and the bacillus coli communis in others.

3. In 80 specimens, representing 17 cases, was found the typical bacillus coli communis.

4. There has now been examined by the different investigators, the urine from nearly 600 cases of typhoid fever. In more than 150 of these cases, at least 35 per cent., the typhoid bacillus was found.

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5. In the greater number of my cases, the typhoid organisms were first found from the end of the third to the middle of the fourth week of the disease. They may, however, make their appearance as early as the twelfth or thirteenth day, as shown in Cases V and VII, or as late as the fortieth day, as shown in Case LIV.

6. Age would seem not to be a factor in the occurrence of the bacillus of typhoid fever in the urine of typhoid patients. In my series of cases, ages ranged from 8 to 43 years.

7. The typhoid bacillus may continue in the urine for several weeks after the temperature of the patient has become normal.

8. The typhoid bacillus, when accompanied by other species, especially the staphylococcus pyogenes aureus, as in Cases XII and LIV, may occur in such small numbers as might easily escape notice.

9. As pointed out by Horton-Smith and Petruschky, the typhoid bacillus may be found in the urine in such large numbers as to render the urine turbid. This is well shown in Cases I, II, III and IV.

10. The largest number of typhoid bacilli in the urine are more likely to be found just after the height of the fever, from which time they usually decreased in number as long as the examinations continued.

11. If it be possible to formulate conclusions from so small a number of cases, a previous attack of typhoid would also seem not to be a factor. In my 65 cases, 4 of the patients had previously had typhoid fever, and in but one of these four, about the usual percentage, was found the typical typhoid bacillus.

12. In the cases examined by me, where the bacillus of typhoid was found, albumin was always present, frequently in large amount.

13. In the cases which contained the typical typhoid bacillus, pus was almost invariably demonstrable, even

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although in many cases no pus microbes were present. This would seem to lend additional support to the theory that the typhoid bacillus may itself under certain conditions be a pus producer.

14. The results here presented, as well as those of other investigators, seem to demand that a systematic bacteriological examination and careful centrifugalization of all urines from typhoid cases should be made.

15. When the typhoid bacillus is detected by this means some measures of prophylaxis against infection should be taken. From the first appearance of the typhoid bacilli, until they disappear, rigid disinfection of the urine should be practiced.

The ideal prophylaxis would be attained by preventing the development of the typhoid germs in the urine. One means of accomplishing this result would be the administration to the patient of small doses of urotropin, as first recommended in these cases by Richardson.

In conclusion, I wish to say that I am indebted to Prof. E. O. Jordan for many valuable suggestions given during the progress of the work. To Prof. Ludvig Hektoen, and to the house staffs at Cook County, Michael Reese and the Presbyterian Hospitals, I wish also to express my gratitude for the material used.

May 14, 1900.

PATHOLOGY AND PATHOGENESIS OF BUBONIC PLAGUE.

LEWELLYS F. BARKER.

Gross and microscopic specimens of the buboes and internal organs removed from Chinese, dead of plague,

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in San Francisco, were presented. The demonstration was accompanied by a brief description of the pathology and pathogenesis of bubonic plague. In the bubonic form of the disease the lesions in the lymph glands and surrounding tissues—edema, hemorrhage and necrosis—are very characteristic. The changes in the spleen are more marked in the septicemic form than in the bubonic form. A specimen of spleen under the microscope showed extensive necrosis of the splenic framework and pulp, with wandering in of polymorphonuclear leucocytes.

Primary plague pneumonia is distinguished from aspiration pneumonia and from embolic pneumonia occurring as complications of plague. The enormous number of bacilli present, the abundance of blood in the exudate, and the small part played by fibrin are interesting features.

The question of portal of entry was discussed in connection with the various clinical types, and an effort was made to explain the fact that local lesions in the skin and mucous membranes and lymphangitis are rarely present, the first outspoken lesions occurring in the nearest packet of lymph glands.

May 13, 1901.

THE TOXIC EFFECTS OF FORMALDEHYDE AND FORMALIN.

(A PRELIMINARY COMMUNICATION.)

MARTIN H. FISCHER.

Three guinea-pigs, four rats, a dog and a cat were subjected for varying lengths of time to the inhalation

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of formaldehyde, generated by volatilizing paraformaldehyde pastils in a Schering disinfecting lamp, in a room of 5.5 c.m. capacity. The animals developed a pneumonia, bronchitis and tracheitis which varied in intensity according to the concentration of the gas and the length of the exposure. A beginning pneumonia was found in animals exposed in the room for one and one-half hours, during which time only 3 gms. of paraformaldehyde were volatilized. The pneumonia is primarily eosinophile; the eosinophiles are followed by the other polynuclear leucocytes, and these in turn by large and small mononuclears. The leucocytes are found in the alveolar walls, and in isolated patches filling one or more alveoli. There are accompanying changes in the cells of the parenchyma. vascular congestion and exudation. The bronchi are filled with serum, leucocytes, desquamated and degenerated bronchial epithelium, cellular debris and mucus. The tracheitis is characterized primarily by eosinophile leucocytic infiltration; this is followed by infiltration with the other forms of polynuclear leucocytes and accompanied by vascular congestion and degenerative changes in the bronchial epithelium. Cultures from the lungs, bronchi and trachea were nearly all negative, so that it is believed that the pneumonia is due to the inhalation of the noxious agent, and not to a secondary infection with bacteria.

Eleven animals—rabbits, kittens, and a dog—received injections into the stomach of varying amounts of formalin of strengths varying from 1 per cent. to the concentrated chemical. Sudden death resulted in three animals; one lived an hour, another forty hours; two were killed after a month; the remainder died at varying intervals in from three to nine days. The symptoms following the injection are subject to great variations. There may be scarcely any reaction whatsoever. At other times there are emeses, micturitions, defecations,

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convulsions, depression of temperature, difficult breathing, weak pulse, etc. From the study of this series of experiments it seems that neither the symptoms nor the time of death of the animals depend upon the increase in the amount or in the strength of the injected chemical, retention after ingestion (absence of vomiting), an empty stomach, or the size and weight of the animal experimented upon.

The attempt to get a series of experiments which would show a progressive increase in the severity of the pathological changes with a progressive increase in the strength and amount of injected formalin resulted in failure. Briefly summarized, the histological findings in the eleven stomachs examined are as follows:

Intense vascular congestion. Three cases which died suddenly.

Intense vascular congestion with an acute edema of the submucosa. One case which died an hour after the injection of the formalin.

Infiltration of mucosa with leucocytes, together with positive evidences of gland cell necrosis. The necrotic material is hyaline and stains deep purple with hematoxylin. Two cases.

Gastritis involving the entire wall of the stomach, and characterized by marked leucocytosis, karyorhexis, and gland-cell necrosis. The necrotic material is granular and stained violet with hematoxylin. Two cases.

Marked leucocytosis and evidences of cell necrosis in all the tunics of the stomach, together with an intense fibrinous, hemorrhagic exudation into the submucosa. One case.

No recognizable changes. Two cases, which were killed at the end of a month.

Twelve guinea-pigs, two rabbits, and five dogs were injected with formalin intraperitoneally. The symptoms following the injection of the chemical have fairly constant characteristics.

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Postmortem examination of the animals injected with dilute formalin shows a vascular congestion of the intestinal tract. Slight exudation into the peritoneal cavity follows the injection of 1 per cent. formalin, and this becomes extreme when the concentrated chemical is used. The intestines are contracted, and at the points of irritation variously sized ecchymoses have occurred. In the severer cases the entire thickness of the intestinal wall is soft and blood-soaked. The same is true of the omental fat and the abdominal wall. Fibrin clots are frequently found about the viscera.

Histologically we have to deal with a fibrino-hemorrhagic peritonitis, which varies in intensity according to the strength of the injected chemical. The peritoneal-endothelial cells swell, show degenerative changes, and desquamate, singly or in plates. The muscularis shows various degenerative changes. General vascular congestion prevails, and marked leucocytic infiltration into the intestinal wall, mesentery, and abdominal wall occurs. In the severer cases fibrinous exudation and hemorrhages of a most intense kind are common.

The injection of formalin into the lungs is followed by an exudative, fibrino-hemorrhagic pneumonia, which varies in intensity according to the concentration of the injected formalin. Five experiments were made.

The injection of formalin subcutaneously calls forth an inflammation of the subcutaneous tissues, the most striking feature of which is an exudate which in guinea-pigs may be 3 or 4 cm. in thickness. A myositis results from the injection of formalin into the muscles. The leucocytic infiltration is mainly of the polymorphous variety.

The injection of formalin into the anterior chamber of the eye is followed by an inflammation which fills it with polynuclear leucocytes, fibrin, and a homogeneously staining serum. The same reaction follows, accompanied, however, by a conjunctivitis, when formalin is

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dropped into the conjunctival sac. A single drop of the concentrated formalin is sufficient to permanently injure the eye. The course in these cases is usually as follows: Lacrimation, blepharospasm, and contraction of the pupil follow the introduction of the chemical. After twenty-four hours the pupil is contracted to pinhole size and refuses to dilate after the use of atropin. An intense edema of the eyelids prevents their closure, and the cornea becomes dry and opaque. Histologically we have to deal with a most intense panophthalmitis. The eyelids also show severe inflammatory changes.

Definite changes in the liver follow the injection of formalin, no matter where introduced into the body. The inhalation of formaldehyde calls forth similar changes. These consist of cloudy swelling of the liver cells, vacuolation of the cells, degenerative changes in the nuclei, slight leucocytic infiltration, total destruction of the cells, and focal necrosis.

The most severe changes were noted after the injection of formalin into the lungs or into the stomach, and after the inhalation of the vapors of formaldehyde.

The changes in the kidneys are similar to those noted in the liver.

Slight changes of a pneumonic and bronchitic character occur in the lungs of all animals experimented upon.

The spleen showed an apparent increase in the number of polynuclear leucocytes and an abundance of blood pigment.

The heart showed no changes.

An eosinophilia was found in the bladders of two dogs injected with formalin; and also degenerative and desquamative changes in the bladder epithelium.

Four animals were subjected to chronic formalin poisoning. The results of these experiments will be given later.

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Formalin is either directly or indirectly positively chemiotactic. The tissues which are not infiltrated with leucocytes after the injection of formalin are those which have been so injured by the chemical that an inflammatory reaction is impossible. The leucocytic infiltration in the inflammatory reaction which follows the introduction of formalin into an organ has these general characteristics: The eosinophiles are first to appear; these are followed by the other polynuclear leucocytes; last of all come the large and small mononuclears. The polynuclears are in all cases the predominating leucocytes. These rules also hold good in the trachea, bronchi, and lungs of animals subjected to formaldehyde inhalations. In the localized areas of pneumonia following the inhalation of formaldehyde, the mononuclears may, however, be the predominating leucocytes.

February 11, 1901.

VARICOSE VEINS OF THE RIGHT UPPER EXTREMITY IN A CHILD.

BERTHA E. BUSH.

The subject of varicose veins is so commonplace that the briefest review will serve to bring out the interesting features of the case to be presented to-night.

This little girl is 8 years of age, and has had the present trouble all her life. Her parents are living and healthy and her family history shows no other similar case. One brother and one sister died of acute intestinal diseases, each at the age of 10 months, but both were healthy at birth, and never exhibited any enlargement of

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the superficial veins. The mother, since her first pregnancy, has had slight varices in the left popliteal space. It is stated that during the year preceding the birth of this child the mother underwent great physical and mental strain, first from an attack of typhoid fever, and later through the sickness and death of her older child, six months previous to the birth of this one. According to the mother's statement, the second labor proceeded normally until after the delivery of the head, when an unusually long interval elapsed before the expulsion of the shoulders. No instruments were used and no anesthetic. Four hours later a severe postpartum hemorrhage occurred, with the usual results of syncope and weakness, owing to which the mother did not attend to the child herself, and for more than two weeks was not aware that there was any unusual appearance of the arm. Upon noticing it, she was informed by the nurse and later by the physician that the condition had been present at birth, and that it was due to "broken veins." No treatment was attempted. The child cried much and grew slowly, having always remained somewhat below the average in size and strength. She has never shown cyanosis, dyspnea or hemorrhages, but the mother observes that whenever the child has fever, or is greatly fatigued or excited, the veins of the right arm enlarge and become painful. On her second birthday, the child fell out of her nurse's arms, and sustained a fracture of the bones of the right forearm which did not perceptibly alter the appearance of the veins. She has had whooping cough, measles, chicken-pox and mumps, and one short attack of multiple swollen joints which was treated as rheumatism, but whose exact nature is doubtful. In 1900, just following measles, the right hand and arm became much swollen so that flexion could not be made at the elbow and wrist; rest in bed and elevation of the limb were resorted to and later a sling and bandaging. After the subsidence of the acute symptoms, the

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veins were left somewhat larger than before, particularly at the inner end of the clavicle.

Present Condition: The right upper extremity presents a general enlargement of the superficial veins along the anterior aspect from the thumb to the suprasternal notch, with pouchy dilatations varying in size up to that of a small egg, on the thumb, in the palm, above the elbow and near the sterno-clavicular joint. The veins chiefly involved are the digital veins of the thumb, the veins of the palm of the hand, the radial and median in the forearm, the cephalic and basilic in the arm, and the superficial veins over the right pectoral muscles and the right clavicle; also small branches of the right external jugular as far as an inch and a half above the clavicle. During their course these vessels have a bluish color and an irregular soft nodular feel, and the position of their valves is not readily seen. At the larger dilatations the skin is thinned but there is no bruit or pulsation, except at the neck, where the mass is lifted by the carotid impulse beneath. The radial pulse is weaker on the right side than on the left. The greatest structural changes are observed in the right hand, which is wider and smaller than its mate, and shows a large soft mass occupying the radial side of the palm, and extending between the metacarpals to the dorsum of the hand. On the inner side the first joint of the thumb is covered by a soft mass almost continuous with that in the palm. The first three metacarpal bones are shorter, smaller and more widely separated than those of the left hand. There is no paralysis and the muscles, though relatively weak, enable the child to eat, play, sew and write with the right hand. These masses are mottled and purplish in color, and are not ordinarily tender, but become so when they are much enlarged, as is always the case after violent exercise or during fever. A progressive increase in the size and number of the larger dilatations has been noted since infancy; those

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above the elbow enlarging about four years ago, and those at the clavicle having appeared the most recently.

Outside of the circulatory organs, the examination is practically negative; the lungs, kidneys, spleen and digestive organs are normal. There are no enlarged superficial lymphatic glands—no evidences of inherited syphilis. The child is 46½ inches tall, weighs 44 pounds, and is of an active nervous temperament, but shows no organic nervous disease, general or local. The action of the heart is at all times somewhat irregular, but no endocardial murmurs have been noted. Skiagraphs (recently made by Mr. W. C. Fuchs) do not show any aneurysm or other gross pathologic change. Whether or not there is malformation of the chambers or great vessels is uncertain.

In its exact etiology this case is obscure. There is evidently prolonged obstruction to the return circulation, whether from pressure outside the vessel or thrombosis within it is not sure. There is at least a possibility that some deviation from the normal began early in embryonic development. Intrauterine phlebitis of syphilitic origin has been observed attacking the portal and umbilical veins. Such an inflammatory lesion may have affected the veins of the arm. The late Professor Coats stated that "the tendency to varicose veins is often transmitted by inheritance, so that there may be a certain weakness of the walls, allowing of more ready dilatation from comparatively trivial causes." If such weakness of the walls were present in this case, even slight and partial obstruction at first, either by thrombosis or external pressure, might have permitted the over-distension of the veins at lower points, followed by incompetence of their valves, and gradual extension of the process to the smaller tributaries in the customary manner.

Among the authorities the opinion prevails that errors of development are largely responsible for the production of varix.

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In the literature available I was unable to find a strictly parallel case—that is, a congenital condition limited to one upper extremity.

April 8, 1901.

A DESCRIPTION OF THE APPEARANCES IN FIVE CASES OF DIAPHRAGMATIC HERNIA.

C. A. PARKER.

The comparative frequency with which diaphragmatic hernia is met at autopsy, and the rarity with which the condition is diagnosed during life, make all facts in regard to this very interesting subject well worth careful record. Of 250 cases collected by Leichtenstern, in but five was the ante-mortem diagnosis made. Many congenital cases are of such extent as to be quite incompatible with post-natal existence; yet the evidence of autopsies shows that the number who live and possibly reach adult life is considerable.

The object of this paper is not to present an exhaustive study of the literature of diaphragmatic hernia, but to record the appearances in five cases coming under the writer's observation, with a brief review of the salient features.

Hernia of the diaphragm may be divided into two classes, congenital and acquired, according to time and mode of origin; or, according to structure, into true and false, the former usually having a complete sac, the latter having none.

True diaphragmatic hernia, with a sac, is very rare, as shown by the 276 cases collected by Lacher,[1] of which

1. Deutsches Archiv f. Klin. Med., Bd. 27.

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but 28, or 10 per cent., were of this type, and of the 28, but three were traumatic—a very small proportion, yet such as would be expected from their origin. The congenital form is due to a defect in development of the diaphragm, which may be so extensive as to allow the larger part of the abdominal contents to pass into the thorax and interfere so seriously with the functions of both the thoracic and abdominal organs as to render independent existence impossible. In less severe cases the defect is smaller or of such a nature that the dislocation of the viscera gives rise to no subjective symptoms, and the condition is learned accidentally through a physical examination or at autopsy.

The acquired or traumatic form is usually caused by a shot or stab wound, or indirectly by crushing the thorax or abdomen, or by overaction of the muscle itself, as in vomiting. The direct injury to the viscera by laceration, prolapse, or incarceration, may cause immediate or early death; in less urgent cases the wound may heal and all subjective symptoms subside, though extensive dislocation of the viscera remains with little or no apparent effect upon the general health.

Certain parts of the diaphragm, near the orifices for the passage of the aorta, the œsophagus, and the inferior vena cava, and in the costo-xiphoid region where the muscular and fibrous tissues are thin or deficient, are relatively weak and favor the development of hernia. These are the common seats of true hernia with a complete sac. Defective nutrition due to lesions of the phrenic and intercostal nerves, causing atrophy of muscular fibers, also predisposes to rupture.

The seriousness of a defect or lesion of the diaphragm depends upon the complications due to immediate or remote injury to the adjacent or prolapsed viscera. Between the two extremes of the congenital and acquired cases which are very early or immediately fatal, and those which cause no symptoms, there are all grades of

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disturbance. The subjective symptoms often bear very little relation to the extent of injury or prolapse of viscera, though their intensity suggests the degree of interference with function.

Hernia occurs more frequently on the left side. Bryant, of London, says "rupture of the diaphragm occurs only on the left side," in referring to traumatic cases. The liver on the right side serves as a natural barrier to hernia in that portion. The contents of the hernia may be but a small portion of omentum, or include nearly all the viscera of the abdomen. The most common hollow viscus dislocated is the stomach, next the colon, and then the small intestines. Of solid viscera, the omentum comes first in order of frequency, and then the liver, spleen and pancreas. The great omentum is found more frequently than any other single structure, because of the great range of movement of its free extremity and the tenuity of the tissue.

The subjective symptoms range through various degrees of intensity from immediate collapse and death to occasional attacks of pain or distress in the chest or abdomen. In the traumatic or acquired cases the shock and pain may obscure all other sensations than those directly attributable to the wound itself, with little or no reference to visceral lesions; later, should the injury not prove immediately fatal, the visceral symptoms become more prominent. In the congenital form, the visceral symptoms are always the principal ones; they vary from a slight indigestion with nausea and eructations, due to a displaced stomach or other viscus, to the acute symptoms of a strangulated hernia. Respiratory and cardiac distress may arise from the presence of the hernia compressing the contents of the thorax. The objective symptoms are obtained by the usual methods of physical diagnosis.

An open or contused wound furnishes evidence of a recent injury; a scar, evidence of former trouble. The

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abdomen may be unusually sunken and the thorax more than usually distended. Solid organs may not be recognizable in their usual positions, and auscultation and percussion may fail to locate some of the hollow viscera where they normally should be found, while in the thorax may be found a tympanitic stomach or colon, or the liver. Inversion of the patient may increase the displacement and symptoms. Skiagraphy may furnish valuable aid.

The prognosis depends upon the involvement of the viscera. Many of the congenital cases are still-born, or die soon after birth, while others live in health and comfort to old age. In acquired cases, where many important viscera are injured, death occurs very soon; in others, gradual interference with the functions of the viscera causes a fatal termination at a later period. Some have no further trouble after the acute symptoms subside. Contraction of a circular cicatrix on the prolapsed part of a hollow viscus may cause obstruction and strangulation. Contraction upon a less important viscus, as the omentum, may cause gradual atrophy of the incarceration and spontaneous cure of the hernia.

Treatment is limited to a small percentage of cases, because of the infrequency of diagnosis. It is entirely surgical, and may be prophylactic, curative or palliative. In the recognized cases some present such serious congenital defects that no relief is possible, and in the acquired form the injury to surrounding viscera may cause death from shock and hemorrhage before anything can be done. In a limited number of cases, where symptoms and conditions were such as to demand surgical interference, immediate and late operative procedures have afforded relief. Immediate closure of the wound in the diaphragm, whenever it is accessible, should be done in all cases to prevent hernia. Should the rent be inaccessible and small, the probabilities are, if a hernia forms, that it will be omental, with the prospect of early

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adhesions to the circumference of the hernial ring effectually closing the opening and preventing displacement of important organs. Both the abdominal and thoracic routes, requiring resection of ribs, have been followed in reducing the hernia and closing the wound in the diaphragm.

Specimens from Cases 1, 2 and 3 are in the museum of Rush Medical College, and were, with notes, kindly furnished the writer by Prof. Ludvig Hektoen, who performed the autopsies. Cases 4 and 5 were observed by the writer in the dissecting-room of the same college.

Case 1 was a woman aged 60 years, with a large diaphragmatic hernia formed of the large and small intestines, great omentum and stomach. The left pleural cavity contained, in addition to the lung, the first portion of the duodenum, the omentum and the entire transverse colon, which was adherent to the costal pleura. These structures pass into the pleural cavity, through a circular opening in the left half of the diaphragm, two inches in diameter, located at the anterior junction of the muscle with the left leaflet of the central tendon. The stomach is not twisted upon its axis, but passes into the pleural cavity, fundus first and to the right, and so far up as to drag with it the first part of the duodenum, which lies just external to the esophageal opening of the stomach; this has dislocated the liver toward the left so that the lobus quadratus and gall-bladder lie upon the spinal column; the transverse colon lies in the pleural cavity, the cecum being dragged far to the left, and there are adhesions just below and external to its intrathoracic loop, binding the colon to the costal pleura over the fourth, fifth and sixth ribs in the anterior axillary line. There are no recent changes, no pigmentation and no thickening in any part of the diaphragm, the margins of the opening being smooth and apparently lined by the united pleura and peritoneum. The left lung lies in the upper fourth of the cavity; it is firm, black and heavy;

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the lower lobe is atelectatic, the upper contains a little air. The heart is pushed to the right and lies exactly in the median line.

No antemortem history of the case being obtainable, we know nothing of the symptoms, if any, caused by this condition, nor do we know its origin, whether congenital or acquired. The opening is not in the weak parts of the diaphragm, but is found in what may be considered the strongest part. There were no adhesions around the margin of the opening, no sac, and no evidence of external focal violence, no scar in the skin, and no injury to ribs. These facts, taken with the large size of the opening, two inches in diameter, favor the opinion of the congenital origin of the trouble. From the fact that the transverse colon was the only viscus adherent to the walls of the pleural cavity, it is probable that the other contents of the hernia had more or less freedom as to residence, according to the influence of surrounding conditions, as gravity, abdominal or intrapleural pressure, or variations in contents of the viscera themselves. The portion of the diaphragm preserved shows the large opening with smooth rounded edges and the peritoneum and pleura continuous.

Case 2 was an Italian aged 30, with a traumatic, omental, diaphragmatic hernia. At the postmortem examination there was noted a distinct scar in the left thoracic wall, which later was found to be directly related to the opening in the diaphragm.

Examination of the preserved specimen shows a circular opening in the anterior left half of the diaphragm, about two millimeters in diameter, with thin and smooth edges, having attached to the entire circumference of the opening a hernia of the omentum which projects about eight centimeters into the left pleural cavity (Fig. 1). The abdominal and thoracic cavities were probably entirely separate on account of the above adhesions. The opening in the diaphragm corresponds with the

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scar on the external surface, and the probabilities are that both were produced at the same time and by the same means. The hernia has no sac, is omental, about eight centimeters long and two to three centimeters in diameter, and constricted to two millimeters at the orifice. The clinical history is unknown.

Case 3 was a man aged 35, a laborer, with a traumatic omental, diaphragmatic and intercostal hernia. On examination of the body there was especially noted a scar four centimeters long in the skin, in the anterior axillary line opposite the eighth intercostal space.

In the left muscular portion of the diaphragm, about

Fig. 1, Case 2.—Upper surface of the left portion of the diaphragm, showing the orifice transmitting a part of the great omentum.

four centimeters from its anterior attachment, is a circular opening five millimeters in diameter, with thick, fibrous edges completely filled with a constricted portion of the great omentum continuous with the part below the diaphragm. The omentum is adherent throughout to the ring in the diaphragm, effectually shutting off the pleural from the abdominal cavity (Fig. 2). Lying on the upper surface of the diaphragm is a lobulated mass of great omentum, approximately 4×4×8 centimeters in size, one fringe of which is adherent to the thoracic wall at the eighth interspace in the anterior ax-

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illary line; it extends through an opening 1.5 centimeters long, parallel with the border of the eighth rib at this point, and can be seen extending to the level of the outer surface of the rib, where it terminates in a scar, immediately beneath the scar seen in the overlying skin (Fig. 3). The hernia is composed entirely of omentum and has no sac. No information was obtained as to the nature of the wound represented by the scar.

Case 4 is a large diaphragmatic hernia with the liver and gall-bladder in the right pleural cavity. The subject was a white man aged 50, by occupation a cook, and

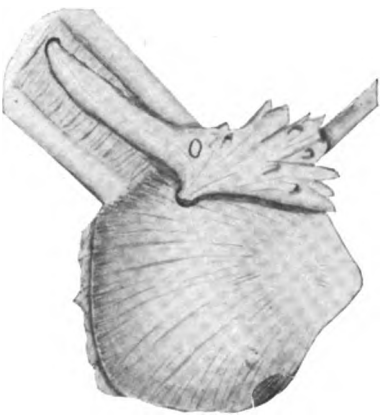

Fig. 2, Case 3.— Upper surface of section of the left side of the diaphragm attached to the eighth and ninth ribs, showing the opening transmitting the great omentum, one prolongation of which extends to an opening through the intercostal muscles and fascia.

fairly well nourished, with no external evidence of local violence on the chest or abdomen. On dissection an old fracture of the sixth and seventh right costal cartilages appeared, union having occurred with some deformity, the accident apparently not affecting the diaphragm at its attachment at that part; there was also an old intracapsular fracture of the neck of the femur of the same side, with good union, and fractures of the right tibia and fibula likewise well united. Whether all of these

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fractures were synchronous I am unable to state, but it is reasonable to suppose that such a severe injury might at the same time produce a rupture of the diaphragm, so that the hernia in question is traumatic rather than congenital. In the central tendon of the diaphragm, involving principally the right leaflet with some of the muscular substance, was an elliptical opening with the long diameter antero-posteriorly, the anterior end being nearer the median line. The opening measured 11.5× 9.5 centimeters, and was partly occupied by the liver, which extended into the right pleural cavity. The border of the opening was free in the greater part of its

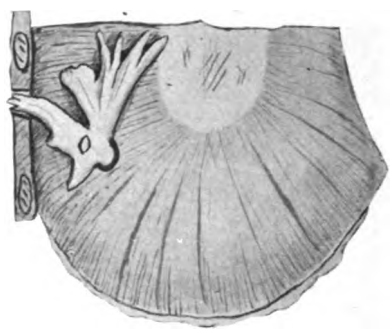

Fig. 3, Case 3.- Same as Fig. 2, showing the portion of omentum extending through the opening between the eighth and ninth ribs.

extent; posteriorly, although easily made out as a cord-like edge, it was covered by the liver and afforded attachment in an irregular manner to its posterior ligament. The border was even and about two millimeters thick, fibrous in structure, and covered by pleura and peritoneum, which were continuous. There was no sac, and the abdominal and right pleural cavities were practically one; the hand could be passed from the abdomen directly up to the right lung and pericardium (Fig. 4). At no place was the margin of the opening nearer than two inches to the attached border of the diaphragm. The opening did not occupy one of the weak places in

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the diaphragm. The hepatic flexure of the colon was hung from the right border of the opening by a firm fibrous band extending from the convexity of the intestine to the pleural surface of the diaphragm. The pyloric end of the stomach with the duodenum was drawn up to the margin of the opening.

The liver measured 15×15×6.5 centimeters and was

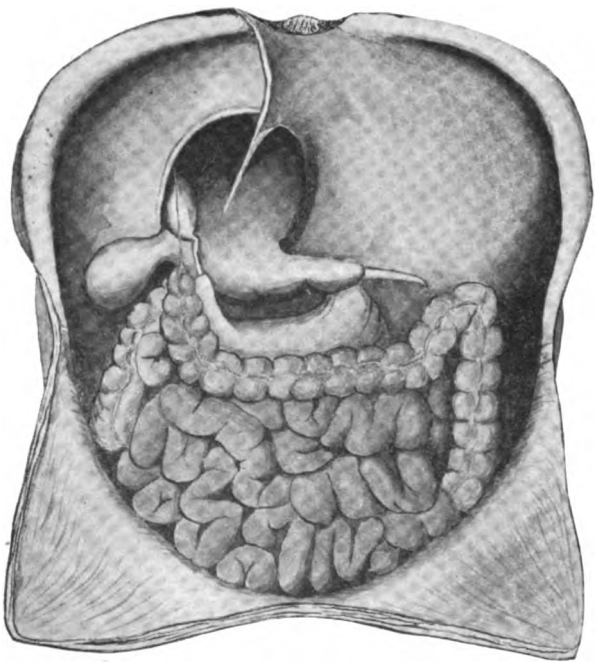

Fig. 4, Case 4.—Diaphragm seen from below with liver and gall-bladder in the large hernial orifice. The round ligament of the liver is seen in the center, and a fibrous cord extending from the hepatic flexure of the colon to the margin of the opening is seen at the left.

somewhat changed in shape by its position. The largest part, involving most of both lobes, was in the right pleural cavity, and so firmly attached by adhesions to the lung and costal pleura that when the subject was placed upright its relation to the diaphragm was not changed.

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The upper border was even with the fourth costal cartilage in front, reaching the fifth and sixth ribs laterally. The anterior border, usually sharp, was uppermost, and

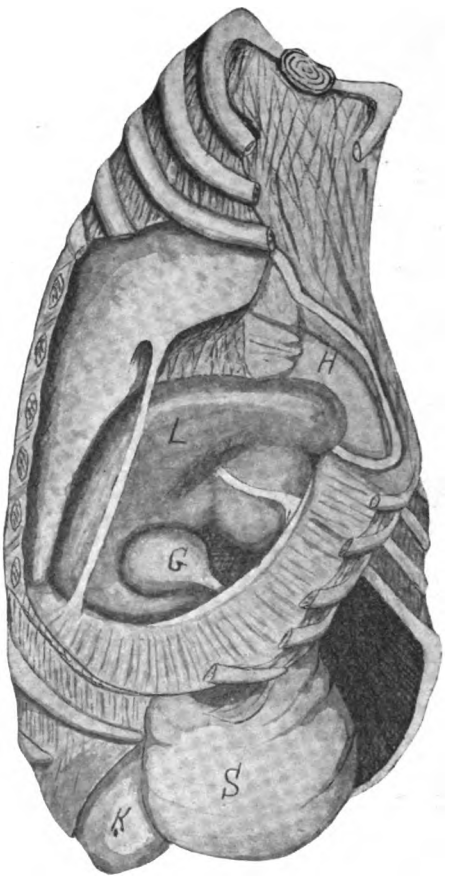

Fig. 5, Case 4.—The right wall of the thorax has been removed, showing the compressed right lung, the heart, and the liver and gall-bladder in the right pleural cavity. The round ligament of the liver is also shown.

thickened like the normal posterior surface; the superior surface became posterior and lay against the posterior thoracic wall, except where a small portion of lung

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substance intervened. The under surface with the gall-bladder was anterior and could be seen through the opening from below. The gall-bladder was normal in size and partially distended with bile; the common duct extended to the duodenum at the level of the opening. The round ligament was free for the first two or three inches from the liver, and was surrounded by the falciform as soon as it entered the abdomen on the under surface of the diaphragm. The right lung extended down to the fourth costal cartilage in front, while behind a narrow lobe extended to the diaphragm, to which it was

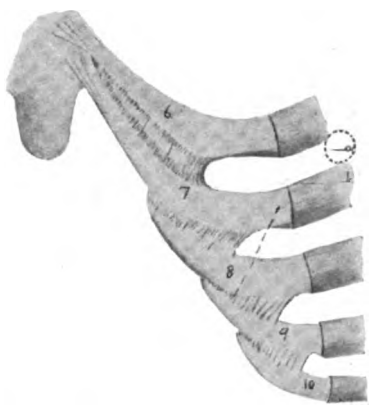

Fig. 6, Case 5.—Sternal portion of ribs and costal cartilages. The dotted line marks the direction and place of severance of the costal cartilages; the circle *a* the position of the intercostal opening.

adherent (Fig. 5). No clinical history was obtained.

Case 5 is a traumatic, diaphragmatic and intercostal hernia. The subject was a man aged 60 years, well proportioned and fairly well nourished. Crossing the left costal arch obliquely upward and outward was a scar about four centimeters long, its outer extremity eight or nine centimeters from the median line, being just over the sixth intercostal space; at this point the palpating finger detected a depression large enough to partially

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receive it; following the scar inward, a marked irregularity of the seventh and eighth costal cartilages was noticed. The skin and fascia were removed, and an opening about one centimeter in diameter was exposed in the sixth intercostal space just under the outer end of the scar and leading directly into the left pleural cavity (Fig. 6). The irregular cartilage had been severed in an oblique direction, with subsequent overlapping of the sternal ends and ultimate firm union in their abnormal positions. Through the opening and lin-

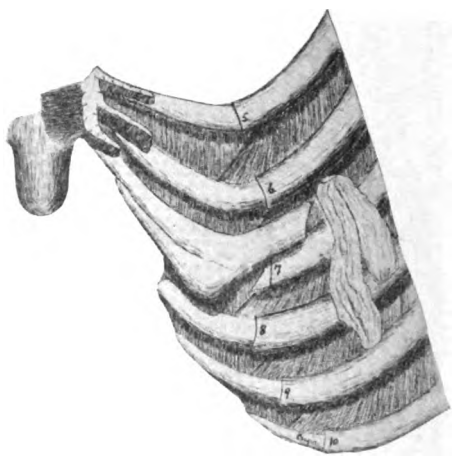

Fig. 7, Case 5.—Sternal portion of ribs and costal cartilages, with intercostal muscles showing dislocated cartilages and a thin vascular tissue, part of an incomplete sac (probably formed of omentum), protruding through the intercostal opening.

ing its margin extended an incomplete sac with thin, muscular walls, which lay between the skin and ribs and for some distance below (Fig. 7). This tissue, followed into the thorax, expanded and was more or less adherent to the pleura and pericardium, and also to the periphery of an opening into the diaphragm. This latter opening was in a direction downward and inward from the intercostal opening and measured 2½x4 centimeters in diameter. It was elliptical in form, on a level

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with the lower border of the seventh costal cartilage, and 1.5 centimeters from the attachment of the diaphragm to the anterior chest wall (Figs. 8 and 9), and was confined to the muscular portion. The margins were thickened and attached to the structures that passed through. As the parts had been disturbed somewhat in dissection, it can not be positively asserted that the pleural and peritoneal cavities were quite separate, but it is believed that they were.

The hernia consisted of the transverse colon, about twenty inches long, its mesocolon with vessels and part of the greater omentum occupying a large part of the left pleural cavity anterior to and to the left of the peri-

Fig. 8, Case 5.—Inferior aspect of diaphragm with hernial opening.

cardium. Numerous adhesions to the surrounding parts gave the appearance of a sac which was not a complete serous structure, nor would we expect a true sac in a hernia produced as this undoubtedly was (Fig. 10). There was no evidence of recent pathological changes in the wound or related viscera, such as might have shortened life.

With no antemortem history we can only conjecture as to the relation of cause and results; it is probable that the wound in the chest wall, severing the two cartilages, and leaving the opening in the intercostal space, was caused at the same time and by the same means as

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the one in the diaphragm; the clean-cut ends of the severed cartilages show it must have been a sharp instrument. Besides the hernia of peritoneum through the intercostal space, the protrusion into the same space of some portion of the large intestine is also probable, an interesting and unusual condition.

As far as is known, these five cases belong to the undiagnosed class. In none was there a true sac. The second, third and fifth were certainly traumatic; the

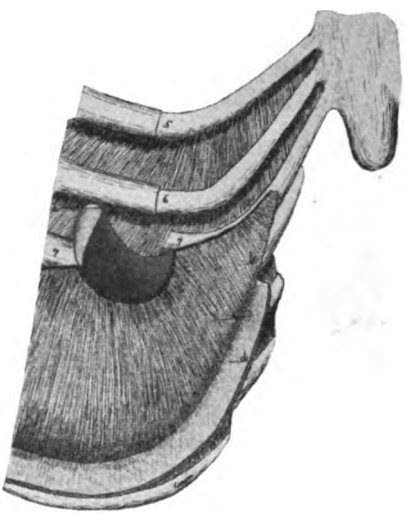

Fig. 9, Case 5.—Internal surface of the chest wall, showing incomplete sac, *b*, extending from the diaphragm to the intercostal opening.

fourth showed in the fractured cartilages evidence of local injury to the wall of the thorax that may have ruptured the diaphragm. There was no evidence of bodily violence in the first case, so that the cause of rupture can only be conjectured. None were in the so-called weak places in the diaphragm. Three were due to stab wounds, and would bear no causal relation to the predisposing factors, and the other two apparently did not. Four were on the left side. As three of these were trau-

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matic, the preponderance of herniæ on the left side in these cases would at first appear to be accidental, although analysis will show it to be due partly to design on the part of an adversary to inflict injury on the heart side, and partly to the fact that the left side is the one directly opposed to the stroke of an opponent's right hand. The relation of the cutaneous scar to the wound in the diaphragm in each of the three cases showed that the thrust must have been from the right hand. The

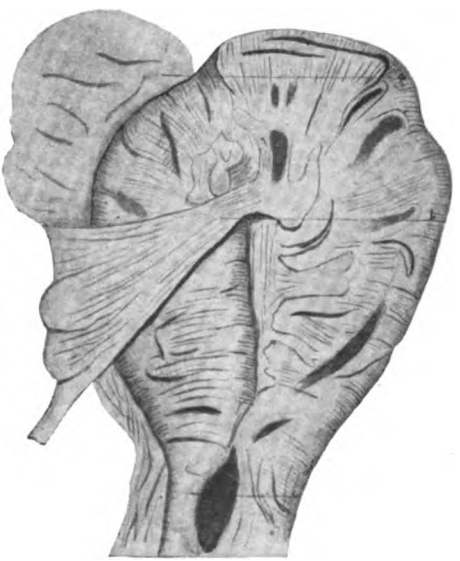

Fig. 10, Case 5.—Hernial contents, loop of transverse colon, portion of sac *a*, transverse mesocolon *b*, and constricted portion of bowel *c*.

contents of the herniæ were the great omentum in four cases, the stomach in one, the colon and mesocolon in two, the small intestines in one, and the liver in one. The omentum was the most frequently displaced viscus, and was the only one in two cases (Figs. 1, 2 and 3). Two were complicated by intercostal hernia, in the sixth interspace in one (Figs. 6 and 7), and in the eighth

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interspace in the other (Figs. 2 and 3). In none was there evidence that the injury to the diaphragm was directly the cause of death, and when it is noted that the three most severe cases—the first, the fourth and the fifth—reached the respective ages of 60, 50 and 60 years, although the herniæ had undoubtedly existed for many years, the indirect or remote effects were slight.

The possibilities of diagnosis in Cases 2, 3, 4 and 5 were much better than in Case 1, because of the local wounds in the former directing attention to the part. The probabilities of complications from narrowing of the hernial orifice were least in Cases 1 and 4, where the openings in the diaphragm were so large that danger of constriction of the contents was slight (Figs. 4 and 5). In Case 5, with the whole transverse colon in the thorax, and the two limbs with the mesocolon passing through an opening $2\frac{1}{2} \times 4$ centimeters in diameter, the danger from constriction was serious, though no apparent interference with the nutrition or function of the part occurred (Figs. 8, 9 and 10). In Cases 2 and 3, contraction had already reduced the openings to a few millimeters in diameter, but as the contents consisted only of omentum, the probabilities are that had the herniæ existed as long as those in Cases I and 4, the prolapsed omentum would have atrophied entirely and spontaneous cure resulted.

Case 5 is especially interesting on account of the probability of a hernia of the large intestine through the intercostal opening, thus doubling the chances for constriction of the bowel. Case 3 was similar as far as the complications of intercostal hernia, but as the contents were omentum only the danger was slight (Figs. 2 and 3).

Probably without treatment directed especially to the diaphragm these five cases lived many years after their injuries. Cases 2 and 3 would not have been materially benefited by operation. No. 4, with the large defect in

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the diaphragm, certainly could not have been helped. Case 1 might have had symptoms that could be relieved by anchoring the abdominal viscera more firmly in their proper position, but closure of the large opening in the diaphragm would have been difficult or impossible. Case 5, with the transverse colon, omentum and mesocolon in the left pleural cavity, might have demanded surgical attention on account of interference with the functions of both the colon and the thoracic viscera. As the bowel and omentum were adherent to the pleura and pericardium and the opening in the diaphragm so small, surgical relief could only have been obtained by a combined laparotomy and thoracotomy breaking up adhesions and possibly enlarging the opening in the diaphragm. It is evident that even were a diagnosis possible in every case of diaphragmatic hernia, in only a very limited number would surgical intervention be practicable or advisable.

The number of cases reported in this paper is quite too small for a comprehensive study of diaphragmatic hernia, yet the data obtained by a careful analysis of the cases cited, supplemented by those of numerous other observers, in the writer's opinion fully justify the following conclusions:

1. Diaphragmatic hernia is of fairly frequent occurrence; the diagnosis is more rarely made than in almost any other known surgical condition, being limited to 2 per cent. of the cases.

2. Absence of a sac is the rule, it being present in but 10 per cent. of all cases, and in only about 1 per cent. of traumatic.

3. Although the so-called weak places in the diaphragm predispose to hernia in some traumatic cases, in shot and stab wounds no such causal relation exists.

4. Stab wounds are usually on the left side because of the desire of an adversary to inflict injury on the heart

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side, and because it is the side naturally opposed to the stroke from an opponent's right hand.

5. The contents of the hernia are most frequently omental, but may include almost every solid and hollow viscus in the abdomen.

6. A complicating intercostal hernia is not infrequent, having occurred in two of the writer's five cases.

7. Though many of the congenital and acquired lesions of the diaphragm are so extensive as to be quite incompatible with life, yet gross defects in its structure, with dislocation of many important viscera, may occur with little or no disturbance of health.

8. The diagnosis is aided by the presence of local scars or lesions directing attention to the diaphragm. Skiagraphy may also be of value.

9. The *immediate* danger in large wounds of the diaphragm is due to injury of adjacent viscera; the *remote* danger, from contraction of the opening and constriction of the contents, is greatest in small wounds.

10. Spontaneous cure may result from contraction of the orifice and atrophy of the contents composed of unimportant structures.

11. The treatment is surgical and is limited to a small percentage of cases, on account of (*a*) the infrequency of diagnosis, (*b*) severity of gross lesions and symptoms, and (*c*) inaccessibility of the part injured.

12. In the examination of all wounds in range of the diaphragm, the possibility of injury to that muscle should be remembered, and all wounds in its structure should be closed at once, if possible, to prevent the development of hernia.

December 11, 1899.

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THREE CASES OF OSSEOUS STYLOHYOID ARCH.

THOMAS R. CROWDER.

The hyoid bars, or Reichert's cartilages, are the skeletal elements of the second branchial arch. They are typically divided into four parts on each side joined end to end, and called pharyngobranchial, epibranchial, ceratobranchial and hypobranchial. The dorsal one of these parts (pharyngobranchial) fuses early with the cartilaginous periotic capsule and becomes, in the adult human, the styloid process of the temporal bone. The second part (epibranchial) becomes partly ligamentous in all placental mammals and wholly so in man, forming the stylohyoid ligament. The third part (ceratobranchial) and fourth part (hypobranchial) both become cartilaginous and ossify early, forming a single piece of bone. This becomes the lesser cornu of the hyoid bone in the adult, which often also contains a small part derived from the second or epibranchial division. The adult hyoid arch then comprises the styloid process of the temporal, the stylohyoid ligament, and the lesser cornu of the hyoid bone.

The body of the hyoid and its greater cornua are derived from the third, or thyrohyoid, branchial arch. The cartilaginous elements of this arch consist primarily of two basihyoids, which fuse and ossify from a single center to form the body of the bone, and two thyrohyoids, which ossify and fuse with the body forming the two greater cornua.

The hyoid bone proper, except for differences in shape and comparative size, is practically a constant structure in the higher vertebrates. There is, however, in the stylohyoid arch much difference in the extent of ossifi-

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cation. In many the arch is completely bony, as in the horse, cow, sheep, elephant. In the dog, cat and other carnivora there is still an almost complete bony arch, but the separate parts are often united by long ligamentous bands to allow of more freedom of motion. The four typical parts are not always distinct in these cases where complete bony arch exists.

It is not unusual to find developmental defects in the hyoid arch of man, more or less of the stylohyoid ligament on one or both sides being represented by osseous tissue. It is, however, comparatively rare to find a complete and symmetrical bony arch exists. It is rarer still to find cases where the four primary divisions of the cartilaginous hyoid bars exist as separate and distinguishable elements, though this is sometimes seen, as in a specimen presented to the Anatomical Society of Paris in August of last year by Sebileau and Gibert. They briefly review the literature of the anomaly, finding the first recorded observation by Serres in 1818.

Two of the three cases of bony hyoid arch presented were recently found in the postmortem room of the Cook County Hospital; the third is an old specimen from the Rush Medical College museum of pathological anatomy. In none of the cases was the condition noted before death, nor did it give rise, so far as known, to any recognizable difficulty. Of one of these cases I am able to present only the fact of its observation, the specimen having been mislaid or destroyed. It concerned a complete bony arch with fibrous articulation at the hyoid ends. I am not able to say that each of the four divisions was present as a separate articulated piece on either side, only that there was no considerable portion of ligamentous tissue. The arch of the second case was roughly removed, and hence mutilated by fracture. It articulated with the temporal at the normal location of the styloid process, with slight or no mobility. In the specimen presented there remains the greater

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part of the epibranchial, a straight, roughly cylindrical bone about five centimeters in length, which represents the normal stylohyoid ligament. The ceratobrachial is also osseous and something less than a centimeter in length. It articulates loosely by fibrous tissue with the epibranchial above, and below with the diminutive hypobranchial or lesser cornu of the hyoid. Or possibly this small division represents the epi- and hypobranchial fused together, hence the whole of the lesser cornu, the fibrous union being directly with the body of the hyoid at the normal location of its lesser cornu. The third specimen has been preserved entire, including a part of the temporal on either side. In this case the separate parts are plainly made out. On the right side the dorsal segment (pharyngobranchial or styloid process) arises from the base of the temporal behind and internal to the vaginal process, as a bony projection 1.5 centimeters in length, the union being osseous and immovable. It is paralleled for half its length by the flattened and elongated vaginal process, and with this it is firmly fused. On the left side the first segment is two centimeters long, and articulates laterally with the vaginal process of the temporal by close, though slightly movable, fibrous union. These upper segments articulate end to end by fibrous union with the second segments (epibranchial or stylohyoid ligaments). There is only very slight motion at this joint. The second segments measure six and five centimeters in length on the right and left sides respectively. The remaining segments are as in the preceding case, the fused cerato- and hypobranchials (representing the lesser cornua of the hyoid), measuring .75 and 1 centimeter on the right and left sides respectively. The union at either end of these bones is a loose fibrous hinge. The hyoid bone presents no gross abnormality of form or position in either of the cases.

This anomaly is to be considered one of development only. It has its origin in the embryonic tendency of

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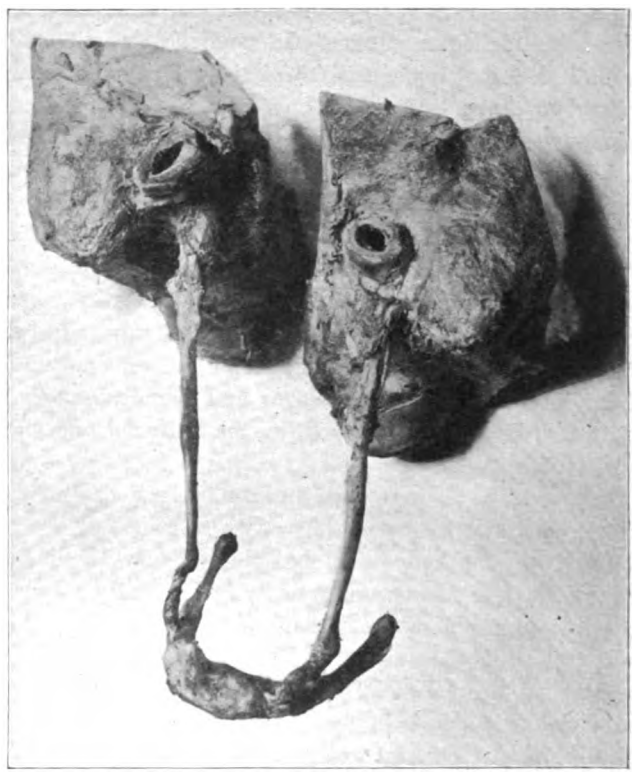
cartilage to ossify, and is not an ossification of the stylo-hyoid arch once developed in the usual way. It is a reversion to a lower type. So far as I know it is interesting from the anatomical standpoint only, and has no



Arch from Case 3.

clinical importance beyond the possibility of fracture and its complications.* The bones being situated deeply

* At the last meeting of the American Medical Association, Dr. Geo. L. Richards reports a case in which the osseous stylo-hyoid arch entered a hypertrophied tonsil, causing long-continued pain and rendering the removal of that organ difficult.—JOUR. OF AM. MED. ASSOC., July 27, 1901.

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in the tissues of the neck and so high up as to be much protected by the lower jaw render this accident improbable.

February 11, 1901.

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CYST-LYMPHANGIOMA OF NECK IN A CHILD.

DANIEL N. EISENDRATH.

The case was one of an enormous tumor of the neck, which was operated upon by myself, the case having been kindly referred to me by Dr. Letourneau. It was almost the size of a child's head when first seen, at the age of six days. Diagnosis made before operation was confirmed, which was a cyst-lymphangioma of congenital origin. The child was operated on when eighteen days old, on account of threatened breaking down of some of the cysts and pressure symptoms on the trachea. Such large congenital tumors are extremely rare, and operative treatment is almost hopeless, as in this case.

November 13, 1899.

RUPTURED RECTUS ABDOMINALIS MUSCLE.

H. G. WELLS.

The specimen was taken from the body of a man who died of lobar pneumonia. There were no evidences of the rupture during life, and no evident cause since the

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patient had not been violent or suffered from convulsions. The rectus muscles, both of which were ruptured, showed a pale, hyaline appearance for some distance from the point of rupture. He also mentioned a case of rupture of the rectus observed at autopsy in a patient who had died of uremia with violent convulsions. Here there were no degenerative muscular changes, either macro- or microscopically.

January 14, 1901.

LYMPHOSARCOMATOSIS IN A SHEEP.

LEO LOEB.

That is probably the first case of lymphosarcomatosis reported in a sheep. There were many non-hemorrhagic nodules of different size beneath the skin and the fascia. There were tumors in the thyroid gland, in the kidney and in the heart muscle. The reticular network was best seen in the skin tumors. At the margin of the advancing lymph cells between the tubules of the kidney no reticulum was present. At other places small spindle-shaped cells were found among the lymph cells. The latter showed many mitoses. In the thyroid many cysts, partially lined with epithelium, were separated by lymphoid tissue. At some places the lymph cells broke through the epithelial layer.

November 12, 1900.

WILLIAM B. WHERRY reported a case of so-called malignant (staphylococcus) carbuncle of the upper lip

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followed by pyemia. A barber, 23 years old, entered Professor Bevan's service in the Presbyterian Hospital on the 7th of February, 1901, and died on the 8th at 11:15 p. m. About a week before his admission he extracted a "dead hair" from his upper lip. This was followed by redness of the lip and swelling which rapidly extended to the side of the face and shoulder. He rapidly grew worse and died with all the characteristic symptoms of septico-pyemia.

The postmortem examination was held twelve hours after death by Professor Hektoen. The anatomical diagnosis is as follows: Acute, diffuse, purulent and necrotic staphylococcus inflammation of upper lip and adjacent parts of face; multiple abscesses and hemorrhagic pneumonic areas in lungs; double fibrino-purulent pleuritis; abscess in spleen; acute splenic swelling; cloudy swelling of kidneys and liver; persistent thymus.

Bacteriologically, a pure growth of the staphylococcus pyogenes aureus was isolated from the lip, heart's blood, pleural exudate, liver and spleen.

Histologically, the lip shows dense cellular infiltrations with foci of necrosis containing groups of cocci which stain by Gram's method. The lung contains many pneumonic and hemorrhagic areas and mycotic emboli. The other organs show the characteristic changes of a severe infectious process.

The dangers of this affection depend chiefly upon its location and the virulence of the infective agent; the prognosis is extremely grave on account of the liability to thrombosis and embolism. The treatment of the early stage which has so far given the best results is excision of the necrotic area and packing with iodoform gauze. After thrombosis and embolism have occurred, treatment at the present time seems to be hopeless.

June 10, 1901.

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W. E. COATES read a paper on the "Parasitic Origin of Tumors," with microscopic demonstration.

January 8, 1900.

EMANUEL FRIEND demonstrated a dermoid cystadenoma removed from a child 2 years of age. The demonstration was accompanied by the exhibition of drawings.

October 12, 1899.

LUDVIG HEKTOEN read a paper bearing on the relation of parasites to carcinoma.

November 13, 1899.

S. E. MUNSON read a paper upon the relation of milk supplies to tuberculosis.

October 8, 1900.

H. T. RICKETTS demonstrated specimens of general blastomycosis obtained from a dog which had been inoculated intravenously with a culture of an organism obtained from a case of blastomycosis of the human skin.

March 11, 1901.

WELLER VAN HOOK presented a knee from a case of septic synovitis and osteo-myelitis.

November 13, 1899.

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LIST OF MEMBERS

Angear, J. J. M., 142 South Western Avenue.
Babcock, Robert H., 103 State Street.
Bacon, Charles S., 426 Centre Street.
Barker, Lewellys F., University of Chicago.
Baum, W. L., 103 State Street.
Bausman, A. B., 580 West Madison Street.
Bevan, Arthur D., 100 State Street.
Billings, Frank, 100 State Street.
Bouffleur, A. I., 1159 Washington Boulevard.
Brennecke, Herman A., Aurora, Ill.
Brophy, T. W., 126 State Street.
Brower, D. R., 597 Jackson Boulevard.
Brown, Sanger, 757 Washington Boulevard.
Bryan, C. J., 1079 Washington Boulevard.
Burgess, A. J., Milwaukee, Wis.
Burwash, Henry J., 721 North Hoyne Avenue.
Bush, Bertha, Rogers Park, Ill.
Capps, J. A., 226 East 53d Street.
Chandler, Ralph, Milwaukee, Wis.
Chapman, C. F., 929 West Monroe Street.
Chapman, George L., 1112 North Clark Street.
Christopher, W. S., 508 Dearborn Avenue.
Class, W. J., 1301 Belmont Avenue.
Cleveland, George H., 951 West Harrison Street.
Coates, W. E., 417 S. 44th Avenue.
Colburn, J. E., 34 Washington Street.
Cook, E. P., Jr., Mendota, Ill.
Cooke, Jean M., 5810 Prairie Avenue.
Coolidge, F. S., 103 State Street.
Corwin, A. M., 301 Ashland Boulevard.
Cotton, A. C., 1485 Jackson Boulevard.
Crowder, T. R., 415 North State Street.
Dal, John W., 499 North Robey Street.
Danforth, I. N., 905 West Monroe Street.
Davis, Thomas A., 979 Jackson Boulevard.
Davis, N. S., Jr., 65 Randolph Street.
Dewey, F. J., 302 South Oakley Avenue.
Diamond, I. B., 294 West Division Street.
Dickerman, Edward T., 103 State Street.
Dodson, John M., 568 Washington Boulevard.

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Doepfner, Karl, 581 Orchard Street.
Doherty, David J., 582 La Salle Avenue.
Dudley, E. C., 1617 Indiana Avenue.
Earle, F. B., 903 West Monroe Street.
Eckley, W. T., 979 Jackson Boulevard.
Edwards, A. R., 103 State Street.
Eisendrath, D. N., 3125 Michigan Avenue.
Engelmann, Rosa, 3035 Indiana Avenue.
Evans, W. A., 103 State Street.
Favill, H. B., 100 State Street.
Fenger, Christian, 269 La Salle Avenue.
Fisher, John, 364 La Salle Avenue.
Fitch, C. M., 645 West Monroe Street.
Fitch, W. M., 645 West Monroe Street.
Fütterer, Gustav, 716 Fullerton Avenue.
Gavin, E. F., Waukegan, Ill.
Gehrmann, A., 103 State Street.
Graham, D. W., 672 West Monroe Street.
Grinker, J., 1047 Milwaukee Avenue.
Grim, U. J., 785 West Madison Street.
Hamill, Edwin, 812 Warren Avenue.
Hamilton, Alice, Hull House.
Hammon, G. M., 683 West Adams Street.
Hanson, Z. P., 376 Warren Avenue.
Harlan, A., Masonic Temple.
Harris, M. L., 100 State Street.
Hartman, F. S., 568 Congress Street.
Harvey, R. H., 2100 Calumet Avenue.
Heineck, A., 872 Trumbull Avenue.
Hektoen, Ludvig, Rush Medical College.
Henke, F. W. E., 524 Ashland Boulevard.
Henrotin, Fernand, 353 La Salle Avenue.
Herrick, James B., 751 Warren Avenue.
Herzog, Maximilian, 174 East Chicago Avenue.
Hessert, William, 685 Fullerton Boulevard.
Heym, Albrecht, 103 Randolph Street.
Holinger, J., 103 Randolph Street.
Hook, E. I., 1522 North Rockwell Street.
Ingals, E. F., 34 Washington Street.
Jay, Frank W., 2510 Indiana Avenue.
Johnson, Frank S., 2521 Prairie Avenue.
Jordan, E. O., University of Chicago.
King, Herbert M., Grand Rapids, Mich.
Klebs, Arnold, 147 Lincoln Park Boulevard.
Kerr, N., 295 La Salle Avenue.
Kohn, Alfred D., 3340 Michigan Avenue.
Kyes, Preston, University of Chicago.
Latham, V. A., Rogers Park, Ill.

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Le Count, E. R., 398 Marshfield Avenue.
Lemke, A. F., 103 State Street.
Lewis, C. J., 733 Carroll Avenue.
Lewis, H. F., 4426 Lake avenue.
Lieberthal, David, 151 Goethe Street.
Linnell, B. M., 290 Belden Avenue.
Loeb, J., University of Chicago.
Loeb, Leo, 452 60th Street.
Loomis, E. B., 145 South Robey Street.
Luken, M. H., 587 West North Avenue.
Lyman, Henry M., 200 Ashland Boulevard.
Marshall, F. D., 679 West Adams Street.
MacMartin, D. R., 77 Jackson Street.
McArthur, L. L., 100 State Street.
McCullough, J. R., 37 Park Avenue.
McDill, John R., Milwaukee, Wis.
McIntyre, C. J., 849 Grand Avenue.
Meling, N. C., 952 Armitage Avenue.
Meyer, Adolph, Worcester, Mass.
Misick, O. S., 445 East North Avenue.
Montgomery, Frank Hugh, 100 State Street.
Moyer, Harold N., 103 State Street.
Mueller, George, 1063 Milwaukee Avenue.
Munson, Samuel E., Springfield, Ill.
Murphy, J. B., 100 State Street.
Newman, H. P., 103 State Street.
Ochsner, A. J., 710 Sedgwick Street.
Ochsner, E. H., 528 Garfield Avenue.
Olney, T. A., 175 Park Avenue.
O'Neill, J. W., 1373 North Clark Street.
O'Shea, D., 470 Ashland Boulevard.
Parker, Charles A., 16 South Homan Avenue.
Patrick, Hugh T., 34 Washington Street.
Peterson, R., 103 State Street.
Pfeifer, John P., 1218 Milwaukee Avenue.
Plummer, S. C., 4304 Lake Avenue.
Preble, R. B., 590 Dearborn Avenue.
Prendergast, Joseph, 1510 Lake Street.
Price, O. J., 538 West Adams Street.
Pritzker, L. J., 547 North Robey Street.
Pusey, Brown, 31 Washington Street.
Pusey, W. A., 103 State Street.
Rhodes, John Edwin, 34 Washington Street.
Ricketts, H. T., Rush Medical College.
Ries, Emil, 100 State Street.
Robison, John A., 297 Ashland Boulevard.
Root, Eliza H., 489 West Monroe Street.
Rumpf, W. H., 100 State Street.

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Ryan, L., 1271 West Van Buren Street.
Sandberg, Karl F., 622 North Hoyne Avenue.
Schaeffer, F. C., 582 Washington Boulevard.
Schalek, Alfred, 34 Washington Street.
Simmons, George H., 61 Market Street.
Sippy, B. W., 3914 Ellis Avenue.
Slaymaker, S. R., 1318 Washington Boulevard.
Somers, G. H., 514 Jackson Boulevard.
Steele, D. A. K., 103 State Street.
Stehman, H. B., Pasadena, Cal.
Stevenson, Alex. F., Jr., Presbyterian Hospital.
Sutton, Emerson M., Peoria, Ill.
Swenson, Carl G., 318 East Division Street.
Talbot, Eugene S., 103 State Street.
Tebbetts, J. H., Hollister, Cal.
Test, Annabel Cleveland, 4401 Indiana Avenue.
Thometz, John L., 999 West 12th Street.
Tice, F., 1044 West Monroe Street.
Turck, F. B., 362 Dearborn Avenue.
Twining, S. D., 210 Grand Avenue.
Van Hook, Weller, 5759 Washington Avenue.
Van Hoosen, Bertha, 489 East 42d Street.
Wagner, Carl, 75 Lincoln Avenue.
Waite, Lucy, 98 Loomis Street.
Watkins, T. J., 3564 Grand Boulevard.
Weaver, George H., 535 Washington Boulevard.
Weber, Samuel L., 100 State Street.
Webster, J. C., 100 State Street.
Wells, E. F., 4571 Lake Avenue.
Wells, H. Gideon, University of Chicago.
Wescott, C. D., 31 Washington Street.
Wesener, J. A., 103 State Street.
Wilder, William H., 103 State Street.
Willson, Charles G., Milwaukee, Wis.
Williams, John C., The Plaza.
Wing, Elbert, 34 Washington Street.
Woley, H. P., 4257 Grand Boulevard.
Worthington, H. C., Oak Park, Ill.
Zeit, Robert F., 4016 Vincennes Avenue.

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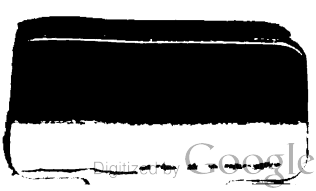

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